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The Journal of Allergy

VOL. 6 JANUARY, 1935 NO. 2

Original Articles

THE EFFECT OF LOW RELATIVE HUMIDITY AT CONSTANT TEMPERATURE ON POLLEN ASTHMA*

B. Z. RAPPAPORT, M.D., TELL NELSON, M.D., AND WILLIAM H. WELKER, PH.D., CHICAGO, ILL.

THE study of the past year was a continuation of the observations made during the preceding two years on the effect of air filtration on pollenosis. During the 1932 season one ward was equipped with a unit for filtering the air free of pollen, while the other was equipped with both a filtration unit and an electric refrigeration apparatus for cooling the filtered air. Our conclusion was that no additional benefit was derived by this means of cooling the filtered air. The increased relative humidity resulting from cooling a rapidly changing air supply seemed to aggravate patients suffering from asthma.

One observation made in our study during the 1932 season[1] was the primary reason for the present study of the effect of controlled humidity on pollen asthma. We observed that even in filtered air giving a settling of only a few pollen grains per cubic yard per twenty-four hours, sudden atmospheric changes produced an attack of asthma in pollen sensitive patients. Seven patients were in the two wards, September 12, 1932. Six of these had been under observation for nine days, and one had been admitted September 11. All had little or no asthma the night of September 11. On September 12 sudden weather changes occurred, namely, a sharp fall in barometric pressure followed by a rise and another fall, a sudden fall in temperature and a sharp rise in relative humidity. Heavy precipitation occurred late in the afternoon and again in the evening. That evening and night all had severe asthma. Five of the seven patients remained in the wards until September 22. It rained again September 20 but the barometric change was not great, rising only slightly and gradually, the relative humidity rose less and the temperature fell. No asthma occurred in any of the five patients on September 20.

*From the Departments of Medicine and Physiological Chemistry, College of Medicine of the University of Illinois, Chicago.

The occurrence of simultaneous attacks of asthma in the seven patients on September 12 with no pollen in the rooms to account for the symptoms brought up the following question: What factors in atmospheric conditions are responsible for the precipitation of attacks of asthma—fluctuations in the barometric pressure, changes in the relative humidity or temperature, or ionic changes? With the equipment used this year, the humidity and temperature in the ward were controlled within very narrow limits. This left two variables to be studied at a later date, the changes in barometric pressure and the atmospheric ionization.

In this year's experiment the installation consisted of five parts: a primary filter, a dehumidifying system, a circulating fan, a cooling system, and a secondary filter.

The primary filter consisted of two fluted cellulose units, 20×20 inches, with a filtering surface of 23.5 sq. ft. per unit. These filters were placed vertically in the filter compartment. All fresh air passed through this filter before dehumidification.

Dehumidification was accomplished by a unit consisting of an absorbing cylinder using silica gel as the absorbing agent, a gas furnace to heat the gel to drive off the absorbed water, a blower to propel the air, and a finned water coil cooler. The absorption cylinder consists of 24 sections, one-half of which were absorbing moisture out of the air, while the remainder were being heated for the removal of the absorbed water. The furnace gases were carried off through a flue to the outside. The dried air left the silica gel unit at a temperature of about 140° to 150° F., and passed through the cooler.

A blower of the Sirocco type was used for moving the air. The dehumidified fresh air was mixed with the return air from the ward in a mixing compartment prior to entering the blower. It was then passed through the main cooler, which consisted of a four-section finned coil, cooled by tap water.

The air was then passed through the secondary filter, which was placed in a horizontal position in the first part of the riser duct. Two fluted cellulose units were used in this filter. They were of the same size and surface area as those in the primary filter. The air was conducted to the ward through a galvanized iron riser duct. The air to be recirculated was drawn down through a similarly constructed duct to the mixing chamber. These ducts were heat insulated.

The volume of air supplied to the ward varied between 2,200 cu. ft. and 1,500 cu. ft. per minute. The cubic content of the ward was 7,260 cu. ft. Throughout the experiment about 70 per cent of the air supplied the ward was fresh and 30 per cent recirculated. The air pressure in the ward was slightly in excess of the atmospheric pressure. This made the sealing of windows and doors unnecessary to prevent the leaking of outside air into the ward.

The velocity of the fresh air through the primary filter was approximately 30 cu. ft. per minute per square foot of filter surface for the first half of the experiment and later when the speed of the air flow was reduced, the velocity dropped to 25.4 cu. ft. per minute per square foot (Table I). This was a reduction in velocity of air flow over our installation of last season when it was 35.4 cu. ft. per minute per square foot for the same ward.[1]

TABLE I

ANEMOMETER READINGS OF AIR DELIVERY THROUGH THE FILTER UNITS

DATE	PRIMARY FILTERS FRESH AIR		SECONDARY FILTERS TOTAL AIR DELIVERY TO WARD		REMARKS
	C.F.M. TOTAL	C.F.M. PER SQ. FT. FILTER SURFACE	C.F.M. TOTAL	C.F.M. PER SQ. FT. FILTER SURFACE	
Aug. 19	1355	30.11	2130	47.33	Machines started.
22	1385	30.77	2210	49.11	
26					Both stages of filters changed.
30	1380	30.66	2200	48.88	
Sept. 5			1505	33.66	New fan pulleys installed. New pulley 7⅝". Old pulley 9⅝". Secondary filter changed.
6	1145	25.44			Primary filter changed.
16					Both stages changed.
28					Both stages changed. Experiment discontinued.

C.F.M. = Cubic feet per minute.
Filtering surface of each filter was 23.54 sq. ft.
Total of filtering surface for each set 45 sq. ft.

As has been pointed out in our previous work, low velocity of the air through the filter greatly increases its efficiency for the removal of pollen. Vibration of the filters, which has a lowering effect on filter efficiency, was overcome by heavy cloth connections between filter compartments and all parts of the installation in which motors were operated.

The temperature of the ward was controlled during the entire period of the experiment. (Fig. 1.) It varied within very narrow limits irrespective of outdoor fluctuations. This was accomplished by passing the air delivered to the ward through two thermostatically controlled, finned water coil coolers.

The relative and absolute humidity varied very little when compared with the wide outdoor fluctuations (Fig. 1). The absorption efficiency of the silica gel unit during the period of observation averaged 68.41 per cent, while the drop in the absolute humidity in our ward as compared with the absolute humidity outdoors averaged 53.58 per cent for the same period (Table II). This difference is due to the fact that

Table II

Absolute and Relative Humidity of Air Before and After Treatment With Silica Gel and Absorption Efficiency of This Dehumidifying Agent: and Absolute and Relative Humidity Out of Doors and in the Experimental Ward and Drop in Absolute Humidity in Air Conditioned Ward as Compared to Out of Doors

Date	Time	Air intake at dehydration unit		After silica gel treatment		Absorption efficiency in per cent	Out of doors		In experimental ward		Drop in absolute humidity in per cent
		Grains H_2O per pound of air	Relative humidity in per cent	Grains H_2O per pound of air	Relative humidity in per cent		Grains H_2O per pound of air	Relative humidity in per cent	Grains H_2O per pound of air	Relative humidity in per cent	
Aug.											
21	9:30 A.M.						96.0	62	38.0	30	60.5
	11:00 A.M.			36.0	17				43.0	32	55.3
	11:30 A.M.								45.0	31	53.3
	5:30 P.M.	89.0	32	44.0	22	50.5					
22	9:30 A.M.	83.0	50	30.0	16	64.0	89.0	70	41.0	30	54.0
23	11:00 A.M.	78.0	46	28.0	12	64.0	77.0	57	37.0	25	52.5
24	10:30 A.M.	84.0	47	34.0	20	62.3	90.0	62	43.0	43	48.0
25	12:00 N.	87.0	53	38.0	22	56.5	99.0	54	50.0	35	49.5
26	10:40 A.M.	72.0	38	25.0	16	65.3	74.0	74	38.0	28	48.8
27	2:00 P.M.	66.0	39	17.0	11	71.2	67.0	67	36.0	26	53.8
28	2:00 P.M.	36.0	27	31.5	19	57.7	75.0	75	36.0	27	51.8
29	10:50 A.M.	64.5	41	26.0	12	59.7	64.0	64	27.5	22	57.0
30	11:15 A.M.	62.0	39	19.5	9	68.5	68.0	68	30.0	22	55.8
31	5:10 P.M.	65.0	39	19.0	13	70.8	65.0	65	30.0	22	54.0

TABLE II—CONT'D

DATE	TIME	AIR INTAKE AT DEHYDRATION UNIT		AFTER SILICA GEL TREATMENT		ABSORPTION EFFICIENCY IN PER CENT	OUT OF DOORS		IN EXPERIMENTAL WARD		DROP IN ABSOLUTE HUMIDITY IN PER CENT
		GRAINS H_2O PER POUND OF AIR	RELATIVE HUMIDITY IN PER CENT	GRAINS H_2O PER POUND OF AIR	RELATIVE HUMIDITY IN PER CENT		GRAINS H_2O PER POUND OF AIR	RELATIVE HUMIDITY IN PER CENT	GRAINS H_2O PER POUND OF AIR	RELATIVE HUMIDITY IN PER CENT	
Sept.											
1	5:00 P.M.	63.0	37	18.0	9	71.4	69.0	44	19.0	19	58.2
2	12:30 P.M.	84.0	50	31.0	16	63.2	86.0	56	40.0	28	53.5
5	5:15 P.M.	72.0	40	6.5	4	91.3	72.0	42	35.5	24	50.6
6	3:30 P.M.	69.0	33	20.5	15	70.6	70.0	28	36.0	23	48.7
7	11:55 A.M.	98.0	46	42.5	28	56.8	97.0	48	53.5	35	44.8
8	9:30 A.M.	89.0	47	32.0	22	64.0	91.0	48	43.0	30	52.8
9	10:25 A.M.	92.0	47	35.0	25	62.0	95.0	47	48.0	33	49.6
11	10:45 A.M.	70.0	42	20.0	16	71.8	72.0	78	34.0	27	52.6
12	9:50 A.M.	59.0	42	15.0	12	75.8	62.0	63	26.5	22	57.2
13	11:00 A.M.	60.0	43	15.5	13	74.3	60.0	68	22.0	18	63.3
14	10:15 A.M.	62.0	47	19.0	16	69.5	56.0	79	26.0	23	53.5
15	12:00 N.	64.5	43	17.5	14	72.8	65.0	80	27.0	23	58.3
16	11:10 A.M.	96.0	60	40.0	28	58.5	99.0	70	46.0	38	53.5
18	11:00 A.M.	44.5	25	9.0	8	80.0	46.5	36	18.0	16	61.3
19	3:00 P.M.	106.0	65	96.0	82	*	66.0	29	91.0	67	*
20	3:20 P.M.	40.0	26	11.5	10	71.3	42.5	41	19.0	17	55.5
21	2:00 P.M.	46.0	28	7.5	8	83.8	48.0	50	23.0	19	52.0
22	3:15 P.M.	83.0	64	33.0	27	60.5	86.0	80	39.0	34	54.6
23	11:20 A.M.	93.0	54	35.0	30	62.5	91.0	63	46.0	38	49.5
25	4:45 P.M.	106.0	64	47.0	38	55.5	106.0	68	57.5	44	45.7
26	11:15 A.M.	89.0	34	38.0	32	57.3	92.0	70	47.5	38	57.3
27	10:00 A.M.	49.5	30	11.5	10	77.0	48.0	55	24.0	20	50.0
28	12:45 P.M.	52.5	37	13.0	9	77.3	59.0	58	24.5	20	58.4

*Silica gel motor, drum bearing burned out and had to be replaced. Unit shut down temporarily.

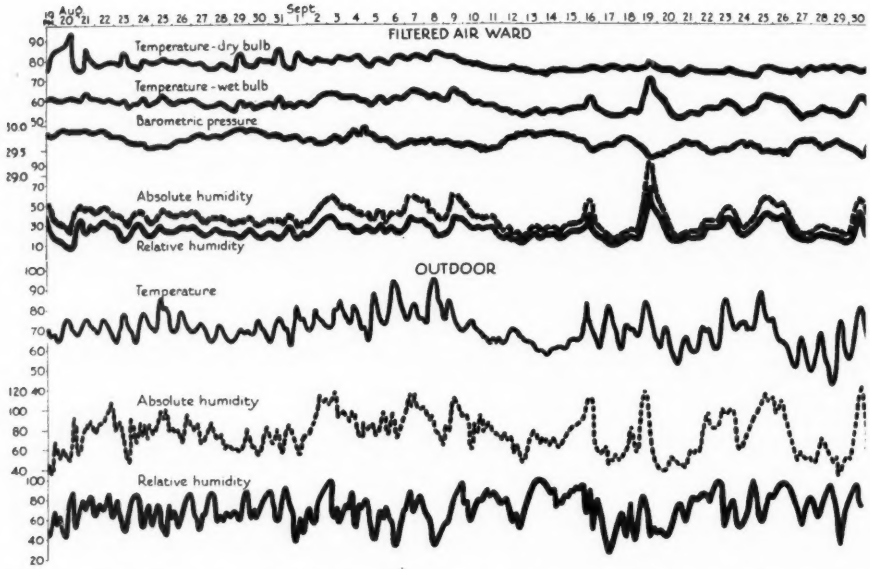
Aug. 19 20 21 22 23 24 25 26 27 28 29 30 31 Sept. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
FILTERED AIR WARD
Temperature - dry bulb
Temperature - wet bulb
Barometric pressure
Absolute humidity
Relative humidity
OUTDOOR
Temperature
Absolute humidity
Relative humidity

Fig. 1.—Chart showing temperature, absolute and relative humidity and barometric pressure in the filtered air ward and out of doors.

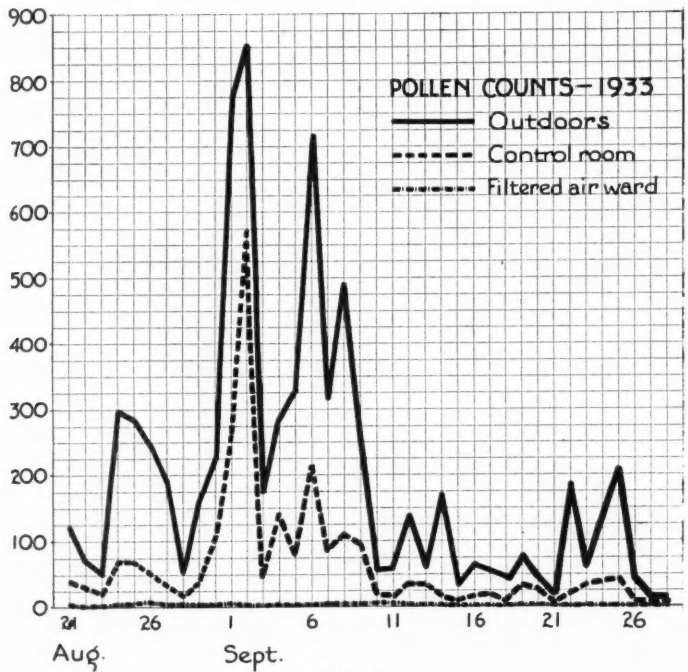

Fig. 2.

30 per cent of the air in the ward was recirculated air which was not again dehumidified.

Pollen counts were made daily from several locations: (a) an outdoor count, (b) in the outlet ducts in the ward, (c) in various locations in the ward and also in a control room of the same size and same general location in the building. The method of counting the slides was the same as that used in the national ragweed survey.[3] As pointed out in our previous work[1] two types of counts were made, one a settling count and one a count in moving air currents (Table III and Fig. 2).

TABLE III

POLLEN COUNTS AND FILTRATION EFFICIENCY OF FILTERING UNITS—1933

DATE	I	II	III	IV	VI	VII
Aug. 21	0	2	0	–	35	123
22	0	1	4	3	–	73
23	0	1	2	1	22	51
24	4	2	1	1	65	297
25	3	2	3	2	65	287
26	0	7	2	7	55	242
27	1	2	4	1	28	190
28	4	5	2	0	17	54
29	1	2	0	0	38	158
30	1	2	0	1	105	228
31	2	4	0	0	265	775
Sept. 1	1	2	2	0	571	850
2	1	3	0	1	49	175
3	4	3	1	0	140	280
4	2	3	3	2	78	326
5	2	4	0	1	210	718
6	6	2	1	2	83	310
7	1	4	0	1	108	487
8	2	4	2	2	95	273
9	7	3	4	1	21	57
10	2	3	0	2	18	61
11	0	3	0	0	33	133
12	3	1	0	1	35	62
13	0	0	0	0	18	170
14	0	1	0	0	9	31
15	0	0	0	0	18	67
16	0	1	0	0	19	54
17	1	1	0	0	9	43
18	0	0	1	0	35	77
19	0	0	0	0	27	40
20	2	2	0	0	5	21
21	0	0	0	0	21	185
22	0	0	1	0	31	58
23	0	0	0	0	–	
24	0	0	0	0	38	205
25	0	0	0	0	7	38
26	0	0	0	0	3	11
27	0	0	0	0	3	13
	50	70	33	27	2,379	7,223

I and II = Settling count in the filtered air ward.
III and IV = Counts taken from intake ducts in filtered air ward.
VI = Settling counts in control ward.
VII = Settling counts out of doors.
Filtration efficiency in comparison to outdoor pollen counts 99.17 per cent.
Filtration efficiency in comparison to control room pollen counts 97.48 per cent.

The slides exposed in the ward were surprisingly free from lint and dust. This was undoubtedly due in a great measure to refiltration of part of the air in the ward. The screen at the intake of the return duct became very quickly coated with lint and dust and had to be frequently brushed clean. This lint was filtered out by the secondary filter, which at the end of a week's continuous operation had a thick evenly distributed coating of lint.

The filtering efficiency of our filtration unit during the entire period of observation was as follows: In comparison to the amount of pollen outdoors, an efficiency of 99.17 per cent was obtained while in comparison to the control ward, the efficiency was 97.48 per cent. This was a decided improvement over previous years[1, 2] and was attributed to a larger filtering surface with lower velocity and to the recirculation of part of the air.

Twenty-eight patients were selected for our study. All gave a history of attacks of asthma for many years during August and September only and had positive skin reactions to the ragweed pollens. Three of the 28 were found unsuitable because of the shortness of their stay and are not considered in this report. The other 25 were confined for periods varying from five to thirty-one days. Only one patient was observed for the short period of five days, two for six days and the rest from seven to thirty-one days.

The purpose of the long period of observation was to determine the effect of weather changes on the symptoms after the patients had improved or had become free of asthma while confined to the ward. With this in mind, the patients were examined and questioned by one of us three times a day.

TABLE IV

DISTRIBUTION OF TWENTY-FIVE POLLEN ASTHMA PATIENTS ACCORDING TO THE SEVERITY OF SYMPTOMS AND THE TIME REQUIRED FOR COMPLETE RELIEF

SYMPTOMS ON ADMISSION	NO. OF PATIENTS	TIME REQUIRED FOR COMPLETE RELIEF							
		1 DAY	2 DAYS	3 DAYS	4 DAYS	5 DAYS	6 DAYS	18 DAYS	NO RELIEF
Severe Asthma	8	0	3	0	1	0	1	1	2
Moderate Asthma	9	1	1	4	1				2
Mild Asthma	5	5							
No Asthma	3								

Confirmation was obtained of previous observations that even in almost pollen free atmosphere the symptoms of asthma were relieved slowly.[1] As shown in Table IV the more severe the asthma the longer it required for complete relief. Two of those admitted with severe asthma failed to be completely relieved, one (Patient 14, Fig. 3) after eight days of strict confinement in the ward, the other (Patient 7, Fig. 3) after thirteen days in the ward, with strict confinement only during the first four days. Two others (Patients 18 and 20, Fig. 3), admitted with

moderate asthma, failed to be completely relieved after eight days of strict confinement. Table IV shows that the time required for complete relief of asthma symptoms was directly proportional to the severity of the symptoms. All who were admitted with mild asthma were free of symptoms in twenty-four hours or less. It should be noted, however, that while it required a long period to clear most of the patients com-

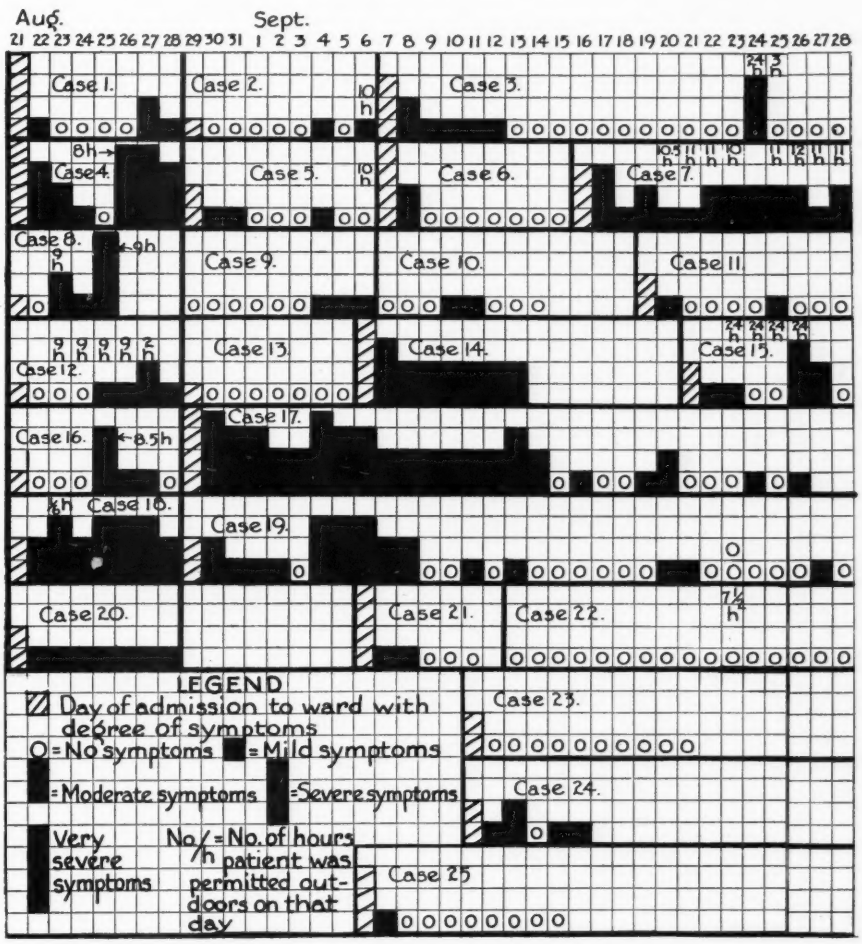

Fig. 3.—Graphic summary of the symptoms of twenty-five patients with pollen asthma confined to the air-conditioned ward.

pletely of asthma, a considerable degree of relief was obtained by the majority of patients in twenty-four hours or less, and by all except one (Patient 18, Fig. 3) in forty-eight hours of confinement.

A few patients were permitted to go outdoors for eight or nine hours after their symptoms had considerably or completely subsided. The observation was previously made[1] that even in patients free of symptoms rapid recurrence of symptoms developed on going outdoors. This was

confirmed in this experiment as these individuals either developed asthma when symptom free or their condition was definitely aggravated if they had asthma when permitted to go outdoors. This is illustrated in Fig. 3.

Our main interest, however, was the effect of atmospheric changes in the individuals confined in the ward with almost no pollen, with the temperature regulated between 76° and 82° F. and the relative humidity controlled within narrow limits. This left only two variables—the changes in the barometric pressure and the ionic changes in the air.

During the period covered by our study, August 21 to September 28, 1933, there were eight rainy days in Chicago. A heavy thunderstorm occurred on September 4. The barometric pressure had been rising since noon September 3 from 29.6 in. to 29.9 in. by morning of September 4. It continued to rise to 29.94 in., dropping suddenly to 29.75 in. during the afternoon of September 4 before the final rise to 29.98 in.

On this day, there was a definite change in the symptoms of those confined to the ward that day—Nos. 2, 5, 9, 13, 17 and 19. All had been strictly confined to the room since August 29, a period of six days preceding September 4. Five of the 6 had been completely free of asthma for one to six days. The sixth who had been admitted with very severe asthma had obtained very definite relief to a degree that the symptoms were considered moderate for the previous two days. Following the rain and thunderstorm on September 4, 4 of the 6, all of whom had been symptom free, developed asthma. The fifth, whose asthma had been moderate, developed very severe asthma. Only one of the patients (No. 13, Fig. 3) who had been admitted with mild asthma and had cleared completely in twenty-four hours remained free of symptoms after the storm. It is noteworthy that Patient 9 who had been admitted on August 29 with no asthma and who remained free of symptoms until September 4, developed asthma after the storm. However, in the four patients who developed asthmatic symptoms, the onset of these symptoms was delayed from six to eight hours after the storm began. Patients not confined to the ward reported the onset of symptoms of severe grade a short time after the storm. In comparison with the group outside the ward the symptoms of patients in the ward were less severe. This differed from our observations following a similar storm during the 1932 experiment, when marked symptoms appeared within an hour of the onset of the storm. These attacks were severe, and persisted in spite of the use of epinephrine for from one to three days.

Following September 4 there were seven more days of rain, including a thunderstorm on September 26. None of these days, other than September 4, as indicated in Fig. 3, was associated with any uniform change in the symptoms of the six to eight patients confined in the ward.

It appears probable from the observations made on September 4, 1933, and September 12, 1932,[1] that in the presence of an irritated respiratory tract due to previous inhalation of pollen, sudden atmospheric changes will produce asthma in some pollen sensitive individuals.

An attempt was made to determine whether the increase in ozone concentration which occurs during a storm was effective in precipitating asthma. An ozonator was connected with the intake duct during September 24 to 28. No effect was noticed in spite of rain on September 25 and 26.

DISCUSSION

The effect of the factors besides pollen on patients having pollen asthma has received surprisingly little attention. In the extensive treatise on asthma and hay fever by Coca, Walzer and Thommen brief mention of the effect of weather changes on pollen asthma is made in the following sentence: "It is somewhat surprising to note what little attention is given the important meteorological factors by various authors who have attempted to correlate the results of pollen treatment of different years." We know of no actual experimental data regarding the effect on pollen asthma, of changes in humidity, in barometric pressure, in temperature or in air ionization. While all of these factors could not be controlled in our present study, the relative humidity and temperature were controlled within narrow limits in addition to efficient air filtration. The fact that following a storm the attacks of asthma came on much later, were less severe, and cleared up sooner than during a similar storm in 1932 would seem to indicate that some benefit was derived by temperature and humidity control, in addition to pollen filtration. That other factors besides those studied, possibly changes in barometric pressure or in air ionization, or both, are also partially responsible for the precipitation of attacks of asthma seems probable from the fact that attacks did occur after a storm even under the conditions of the experiment.

CONCLUSIONS

1. On the basis of our results this year on pollen asthmatic individuals, which showed that complete relief was obtained in four days in 16 patients out of 22, we are led to conclude that the rapidity with which pollen asthmatic individuals are relieved is greater under conditions of low humidity and relatively constant temperature in pollen-free atmosphere than when the temperature and humidity are not controlled.

2. In a pollen-free atmosphere with the relative humidity ranging between 15 per cent and 40 per cent and the temperatures ranging between 72° and 82° F., patients with pollen asthma had a delayed onset (six to eight hours) of symptoms in attacks precipitated by storms. This conclusion is based on a comparison with the time of onset (one

hour) of symptoms in the patients in our experimental ward in 1932. It is our impression that the asthmatic attacks in the ward during storms were less severe and that the symptoms disappeared much more rapidly as compared to attacks precipitated during the experimental period of 1932.

3. Under our experimental conditions, a concentration of ozone considerably greater than occurs after a heavy electrical storm showed no beneficial or detrimental effects.

4. Some other factor, or factors, outside of pollen, humidity, temperature, or the concentration of ozone must play a rôle in the precipitation of symptoms of asthma in pollen asthmatic individuals. Barometric changes and ionization have not as yet been studied.

We wish to acknowledge the assistance rendered by the People's Gas Light and Coke Company of Chicago in supplying and installing the equipment for the dehumidification and cooling and for the technical assistance rendered during the conduct of the experiment.

We wish to acknowledge the assistance rendered by the American Air Filter Co., Louisville, Ky., in supplying and supervising the operation of the air filter units.

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AIR STUDIES AT HIGHER ALTITUDES*

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STUDIES of the pollen of weeds found in the air during the hay fever season have been made by a number of observers during the past few years. Scheppegrell,[1] Gay,[2] Duke,[3] Wodehouse,[4] and others have made pollen studies at ground levels in their own localities. For the past three or four years Durham[5] has been making extensive studies in conjunction with the weather bureau, attempting a survey on a nation-wide scope.

The spore content of the air has been studied for a good many years by agriculturalists interested in plant disease. That spores may affect the health of human beings has been known for a good many years, but has been generally overlooked by the medical profession. Spores may be described as the seeds of molds. They are infinitesimal in size and are easily carried in the air. It is well known that certain foodstuffs, when left exposed to the air, become moldy. Each mold throws into the air millions of spore grains. Bernton[6] called attention to the rôle that spores may play in producing asthma. Stovall and Bubolz[7] have very recently found the same fact and showed that spores may also produce bronchitis. Gifford[8] described spore infections of the eye and it is now known that there are many other pathologic conditions caused by spores.

Other air-borne substances which affect health include scales or particles from insect wings which Parlato[9] has recently described and has proved that these may be causative factors in some cases of hay fever. Dust also has long been recognized as a factor in disease of the lungs. Bacteria that are air borne and the rôle they play in the cause of disease have not been very thoroughly studied.

The present article was written to show the results of air studies made from an airplane in and about Omaha, Nebraska. This means of spore study of the air has been employed by Stakman[10] and by Meier.[11] Duke and Durham have also used the same method in some of their pollen counts.

I have attempted to study spores, pollen and bacteria in this investigation. Through the courtesy of the Rapid Air Transport Company, several airplane flights were made. Through the ingenuity of Mr. Glenn Riddle, a pilot in the employ of the company, an instrument was devised by which two plates and one slide could be simul-

*Read before the Twelfth Annual Meeting of the Association for the Study of Allergy, Cleveland, June 11, 1934.

taneously exposed from the window of a plane (Fig. 1). The plates used were of glass, approximately four inches in diameter and one-half inch in depth. Each plate consisted of two parts, an upper and a lower, the upper portion fitting snugly over the lower half. The bottom of the lower half of the plate was covered with a thin, gelatinous substance containing material favorable to the growth of spores in one case and favorable to bacterial growth in the other. Ordinary glass slides used for microscopic purposes in all laboratories were used. These were covered with a very thin coating of white vaseline so that the pollen grains coming in contact with the surface would adhere. An exposure, then, consisted of removing the covers from the two dishes and putting into place a glass slide. The instrument was exposed outside the plane, withdrawn, and the plates immediately covered and sealed. The plates were allowed to incubate for forty-eight hours for proper identification of the growths. The first ex-

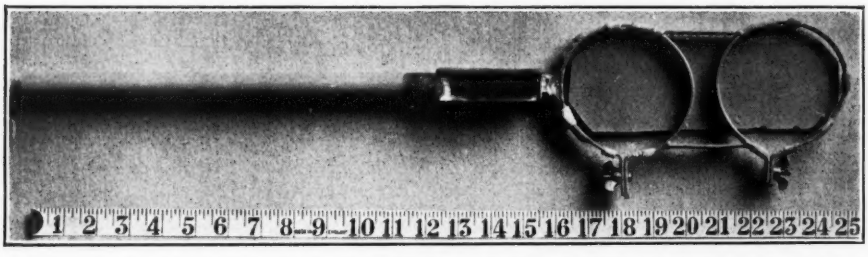

Fig. 1.—The device which makes it possible to expose two plates and one slide.

posures were for five minutes, but because of the tremendous amount of growth obtained, the exposures were shortened to three minutes.

The first exposures were made on a flight from Omaha to Kansas City, Mo. Accurate counts were not done on this occasion because I questioned my technic. The general results obtained on this flight were that pollen, bacteria and spores materially decreased in number between 4,000 and 5,000 feet elevations. Below that level, however, there was very slight difference between the plates exposed. Exposures were conducted up to 7,000 feet.

TABLE I

ELEVATION	BACTERIAL COLONIES	MOLD COLONIES	POLLEN PER SQ. CM.	WIND DIRECTION	WIND VELOCITY
Average counts of three exposures				Surface SSW	12 MPH
3,000 feet	423	Innumerable	167	SSW	25 MPH
4,000 feet	36	Innumerable	38	SSW	24 MPH
5,000 feet	51	18	17	SSW	24 MPH
6,000 feet	2	9	11	SSW	23 MPH
7,000 feet	7	10	9	SW	26 MPH

NOTE.—Counts on plates exposed at one and two thousand feet were practically identical with those of plates exposed at three thousand feet.

The second flight was a repetition of the first and Table I shows the results obtained. Table I definitely indicates that the bacteria decreased materially between 3,000 and 4,000 feet, with a further decrease occurring between 5,000 and 6,000 feet. The decrease in the number of spore colonies occurred betwen 4,000 and 5,000 feet, while the big decrease in the pollen granules occurred between 3,000

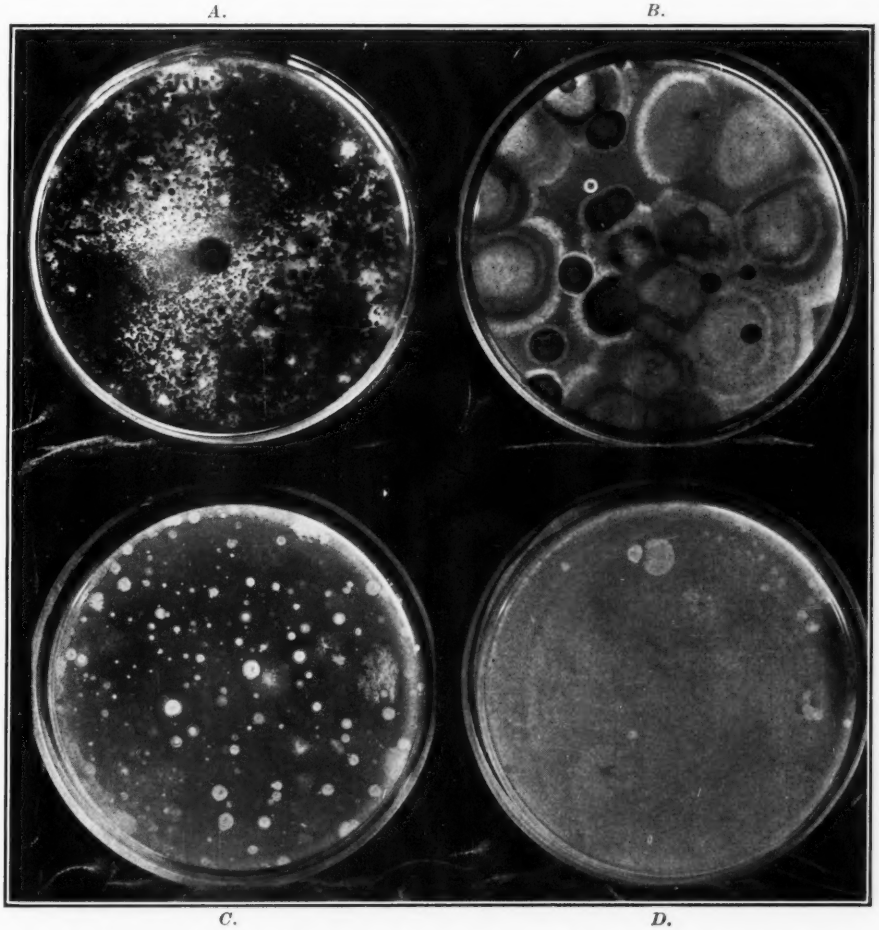

Fig. 2.—*A*, Spore plate at 3,000 feet; *B*, spore plate at 5,000 feet; *C*, basterial plate at 3,000 feet; *D*, bacterial plate at 5,000 feet.

and 4,000 feet. Table I records the results obtained on the flight from Omaha to Kansas City, September 6, 1934.

Fig. 2 illustrates the difference between the exposures at the 3,000 foot level and the 5,000 foot level.

It was an interesting observation that pollen found on this trip at the level of 5,000 feet and above was one with which I am not familiar and I feel certain that it was not a local pollen. The local pollen

disappeared at the 4,000 foot level. It is possible that this pollen was carried from the south, as on the day previous to this flight a storm had occurred over a portion of Texas, and the wind encountered at these higher levels was from the southwest.

The next flight was made between Omaha and Sioux Falls, S. D. Table II shows the result of this flight. It will be noted in the morning flight that the bacteria and the spores were materially less than in the afternoon. The geographic site of the exposures was approximately Sioux City, Ia., for the morning trip. These exposures were made very shortly after a heavy rainfall. The cloud bank extended from the 8,000 foot level to about 1,000 feet. It is entirely possible that the rain clouds were responsible for the small counts. The second exposures for the day were made immediately upon leaving Sioux Falls, where there had not been rain for at least two days and our plates show a marked increase over the morning exposures. The most unusual finding on the entire trip, however, was the 7,000 foot mold, or spore, plate. At this level we obtained hundreds of colonies of one particular spore on the plate, showing the enormous numbers that can be encountered at this high level. Just why this particular spore should have been carried in such large quantities to such a height without mixture of other spores, I am unable to explain at this time.

TABLE II

ELEVATION	BACTERIAL COLONIES	MOLD COLONIES	POLLEN PER SQ. CM.	WIND
A.M.				
1,000 feet	22	272	Not made	Direction and velocity unobtainable on account of cloud banks
2,000 feet	20	90	Not made	
3,000 feet	21	36	4	
4,000 feet	Clouds	Clouds	Clouds	
5,000 feet	4	18	1	
6,000 feet	26	11	0	
7,000 feet	1	8	0	
P.M.				
1,000 feet	145	Innumerable	21	
2,000 feet	400	Innumerable	14	
3,000 feet	240	Innumerable	7	
4,000 feet	Clouds	Clouds	Clouds	
5,000 feet	47	400	3	
6,000 feet	40	130	0	
7,000 feet	18	Innumerable	0	

No effort, in this article, is made to describe or identify the various pollens, spores and bacteria obtained. Other flights have been made, using various types of media to find out, so far as possible, what general classes of bacteria may be found in the higher altitudes. The results of these and of subsequent flights will be given in a subsequent communication.

CONCLUSIONS

1. Pollen of the country surrounding Omaha is found in large quantities up to and including an elevation of 3,000 feet during the pollinating season.

2. Bacteria and spores in almost unlimited quantities are carried to approximately the same height as pollen.

3. Bacteria and spores were carried as high as our studies were conducted, but in decreasing numbers, above the 4,000 foot level.

4. Our counts were affected by the atmospheric conditions encountered.

The writer wishes to acknowledge his debt of gratitude to the Rapid Air Transport Company, as well as to Dr. John T. Myers and Paul Bancroft, University of Nebraska Department of Bacteriology, for their assistance in this work.

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THE POLLEN CONTENT OF THE AIR IN NORTH AMERICA*

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QUANTITATIVE methods of studying the exposure of the public to causes of disease have long been applied to the water we drink and the food we eat, but only recently to the air we breathe. Atmospheric pollen study, as introduced by Blackley,[1] is now recognized by the medical profession as a valuable method of attacking general, local and specific personal hay fever problems.

Fifty-nine years ago this autumn Dr. Marsh of Paterson, N. J., by essentially the same atmospheric methods now used, demonstrated the presence of ragweed pollen in the air in his own city and in New York City. His records for 1875 and 1876 constitute the first atmospheric pollen records for North America.[1] Dr. Marsh's study seems to have satisfied every one concerned for the next forty years, as there is no evidence of any work of this kind having been attempted again until 1916. Then for several years Dr. Scheppegrell studied the pollens in the air in New Orleans,[2] mostly for the purpose of determining the buoyancy of various types of pollen and the effect of weather factors on their distribution. Since 1925 many local atmospheric pollen studies have been made, each for the purpose of a better understanding of the kinds, quantities, seasons, and relative importance of local air-borne pollens encountered by hay fever patients.[3]

A national atmospheric pollen survey first suggested in 1928, was the outgrowth of an attempt to compare several local ragweed records made in different localities by different persons.[4] With the valuable cooperation of the weather bureaus of the United States, Canada, and Mexico, in securing uniform exposures and the indulgence of the Abbott Laboratories in financing the study, I have for the past five years been able to apply the atmospheric method on a national—almost continental—scale. For the first three years almost the whole effort was spent on ragweed,[5] determining its area of distribution, seasons of pollination, and comparative incidence in typical localities. The number of locations studied has been increased from 28 in 1929 to 53 in 1933, the survey eventually spreading into Canada and Mexico. During the past two years all pollens have been counted and recorded,[6] and in the western states exposures were started last year on July 1 in order to obtain a complete picture of the Russian thistle season.

*From the Botanical Laboratories, Abbott Laboratories.
Read at the Twelfth Annual Meeting of the Association for the Study of Allergy, Cleveland, June 11, 1934.

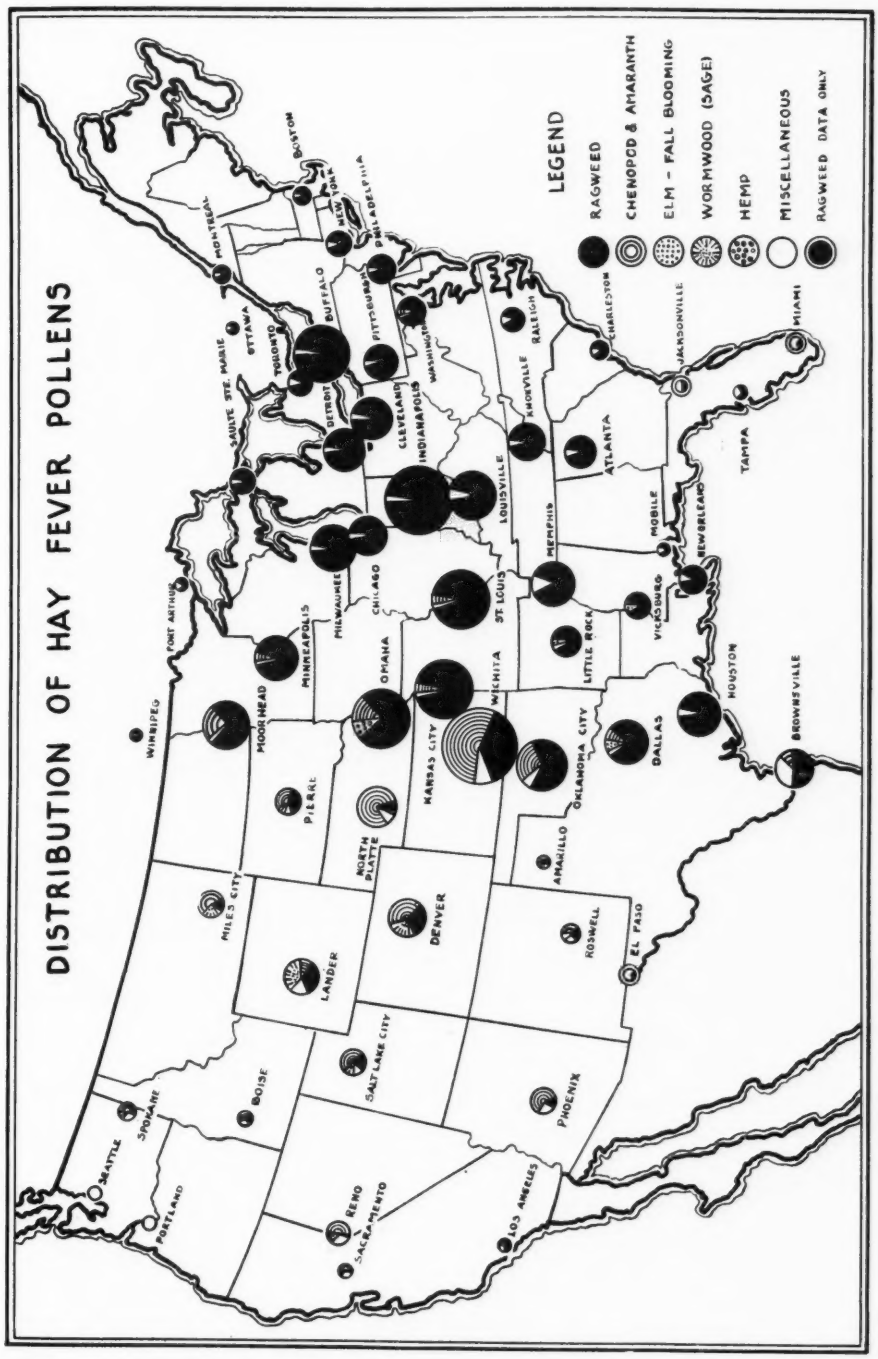

Fig. 1.—The relative area of the discs represents the totals of all late summer and fall pollen found in the air in each city. The key indicates the proportion of the various kinds of pollen found in each place. Thus Wichita had the heaviest average total pollen crop, less than half of which was ragweed. At Indianapolis the pollen content of the air was 98 per cent ragweed. At Seattle and Portland there was no ragweed, and comparatively little of any pollen.

TABLE I

REPORT OF POLLENS FOUND ON ATMOSPHERIC SLIDES IN OMAHA; 1933

	RAGWEED	BURWEED MARSHELDER	RUSSIAN THISTLE	KOCHIA	CHENOPOD AMARANTH	GRASS	HEMP	SAGE (ARTEMESIA)	MISC.
Aug.									
1	2				9	2	23		
2	1				2	2	4		
3	3				3		31		
4	2				2		21		
5	6				15		96		4
6			8	2	24	6	54		
7	10		5	2	7		67		2
8	2		8		4		44		6
9	16				6	4	60		
10	10		38	2	10	10	84		4
11	8		14	10	20	4	94		6
12	30		26		14	4	70		16
13	54		6	2	2	4	100		
14	32		10	2	12		100		2
15	62		4	6	18		128		8
16	64		18	4	14	4	78		10
17	100		42	4	38	4	32		6
18	96		16	2	10		70		2
19	134	1			8	9	25		8
20	118			4	12	5	43		8
21	170			7	5		57		4
22	105				25	1	15		6
23	75		2	6	17	3	43		5
24	147	1	8	2	21		27		5
25	120		6	6	30		32		
26	328	32	2	7	25	11	22		11
27	168	5	2		15	2	2		5
28	640	28	2	3	13	13	18		5
29	748	6	3	5	17	6	5	1	1
30	389	35			17	2	15		9
31	625	35	3	3	30	6	10		17

Thus, with more than 13,000 uniformly exposed slides from 70 cities, representing practically every state in the Union, we were able to evaluate the various hay fever pollens of regional and general importance during the summer and fall. In some cases the stations are five hundred miles apart, and it is altogether likely that many interesting local situations have not been covered. It is believed, however, that these will not seriously change the general picture here presented of the geographical distribution and pollinating habits of the more important groups of summer and fall hay fever plants.

The "gravity" method of securing quantitative samples of the pollen content of the air has been described in my previous papers, and by others who have made similar investigations. Its great advantage in the present study is its simplicity, enabling scores of untrained and busy collaborators to make reliable uniform exposures. The examination of slides has also been fully described in my previous papers.

TABLE I--CONT'D

	RAGWEED	BURWEED MARSHELDER	RUSSIAN THISTLE	KOCHIA	CHENOPOD AMARANTH	GRASS	HEMP	SAGE (ARTEMESIA)	MISC.
Sept.									
1	210			20	10				5
2	382		2	1	34	11	5		6
3	203	1	1	1	49	3	7		3
4	303	5		5	58	8	10		11
5	305			6	57	15	3		8
6	277	5		11	88	9			12
7	537	6	2	5	80	14	10		31
8	230	8	5	2	82	13	3		8
9	119				45	3			4
10	198			6	75	5	2		13
11	143		1	1	29				7
12	8								
13	17								
14	12								
15	22					1			
16	14				7	4	2	1	4
17	22				8	4		2	2
18	80		3	1	12	2		3	4
19	58		2		10				
20	15				4	2			
21	55		2		22	6		2	2
22	2				3	2		1	
23	2				4			1	
24	75				11	5			
25	35				4				
26					1				
27	1				2	1			
28	1				1				
29	5				2	4			
30									
31									

More painstaking identification of species would be desirable—for example, the differentiation of the pollens of short ragweed from giant ragweed—but the effort to lay a foundation has consumed all the spare time and most of the eye energy of one person, and the less important details can be worked out later.

THE RAGWEED AREA

The ragweed belt (Fig. 1) is bounded roughly by the Great Lakes, the Appalachian Mountains, the Gulf of Mexico, and the hundredth meridian, with heaviest recorded production in Indiana. In this area are found ideal conditions of soil, rainfall, open land, and proper length of growing season for full ragweed development.

Outside this area of intensive production various factors result in diminishing ragweed output. The wooded sections of the Appalachian Mountains allow only small acreage to ragweed. The character of

TABLE II

RAGWEED POLLEN TOTALS AND AVERAGES

	TOTAL NUMBER OF POLLEN GRANULES FALLING ON SLIDE AREA (1.8 SQ. CM.) EACH SEASON						POUNDS PER SQUARE MILE
	1929	1930	1931	1932	1933	AVERAGE	
Amarillo, Texas			98	163	178	146	9
Atlanta, Ga.	1,437	1,284	2,408	3,243	3,376	2,350	149
Boise, Idaho	332				209	270	17
Boston, Mass.	582	707	1,169	796	697	790	50
Brownsville, Texas			3,496	2,042	402	1,980	125
Buffalo, N. Y.	4,202	3,948	14,675	12,386	9,751	8,992	568
Charleston, S. C.			373	716	624	571	36
Chicago, Ill.	4,132	3,046	5,018	6,020	7,249	5,093	322
Cleveland, Ohio	3,214	2,646	5,184	4,892	7,720	4,731	299
Dallas, Texas	4,634	2,569	3,606	8,176	4,672	4,731	299
Denver, Colorado	1,767	675	965	1,059	3,804	1,654	105
Detroit, Mich.		2,193	3,901	5,547	8,011	4,913	310
El Paso, Texas	110					110	7
Houston, Texas		5,278	4,055	6,070	8,440	5,961	377
Indianapolis, Ind.	11,439	7,115	9,998	14,409	22,402	13,073	826
Jacksonville, Fla.		205				205	13
Kansas City, Mo.	12,806	4,055	5,492	9,187	8,844	8,077	510
Knoxville, Tenn.		2,782	3,254	4,008	3,777	3,455	218
Lander, Wyo.					1,333	1,333	84
Little Rock, Ark.			2,024	2,776	1,714	2,171	137
Los Angeles, Calif.	32				144	88	6
Louisville, Ky.		3,934	11,355	6,438	8,240	7,492	473
Memphis, Tenn.	4,580	2,977	3,623	5,112	5,325	4,323	273
Mexico City, Mex.				39	29	34	2
Miami, Fla.	8					8	0.5
Miles City, Mont.	248				190	219	14
Milwaukee, Wis.			7,458	5,073	7,151	6,561	415
Minneapolis, Minn.		2,596	3,674	6,984	8,567	5,455	345
Mobile, Ala.			228	507	651	462	29
Montreal, Canada		439	740	806	991	744	47
Moorhead, Minn.	6,267	3,501	3,946	3,995	5,724	4,687	296
New Orleans, La.	1,090	1,982	1,350	2,533	3,832	2,157	136
New York, N. Y.	1,196	1,100	2,643	1,451	1,639	1,606	101
North Platte, Neb.		722	372	831	840	691	44
Oklahoma City, Okla.	6,309	3,360	3,115	3,306	7,483	4,715	342
Omaha, Neb.	12,085	3,790	5,936	11,207	7,554	8,114	513
Ottawa, Canada			459	623	543	542	34
Philadelphia, Pa.	1,799	2,040	3,514	2,185	3,496	2,607	165
Phoenix, Ariz.					145	145	9
Pierre, S. D.		388	313	1,199		633	40
Pittsburgh, Pa.	2,499	1,828	5,734	2,756	6,547	3,873	245
Port Arthur, Canada			226	378	331	312	20
Portland, Oregon					0	0	0
Prince Albert, Canada		6				6	0.3
Raleigh, N. C.	557	929	1,786	1,078	2,352	1,340	85
Reno, Nevada					12	12	0.8
Roswell, N. M.					350	350	22
Sacramento, Calif.					34	34	2
St. Louis, Mo.	5,686	3,487	5,573	8,619	11,293	6,932	438
Salt Lake City, Utah		313			282	297	19
Sault Ste Marie, Mich.	500					500	31
Seattle, Wash.	0					0	0
Spokane, Wash.					8	8	0.5
Tampa, Fla.			582	636	472	563	36
Tampico, Mex.				279		279	18
Toronto, Canada		581	1,357	1,600	1,468	1,251	79
Vicksburg, Miss.			1,355	1,528	2,111	1,665	105
Washington, D. C.	1,956	1,241	3,933	1,497	2,637	2,253	142
Wichita, Kansas	10,123	3,979	4,009	6,406	2,686	5,441	344
Winnipeg, Canada		130	252	278	836	374	24

TABLE III

POLLEN CONTENT OF THE AIR DURING JULY, AUGUST AND SEPTEMBER. AVERAGE FOR 1932 AND 1933

	BURWEED MARSH ELDER	ALL OTHER RAGWEEDS	TOTAL RAGWEED	PER CENT OF GRAND TOTAL	RUSSIAN THISTLE	KOCHIA	MISC. CHENOPOD AMARANTH	TOTAL CHENOPOD AMARANTH	GRASS	ELM (FALL-BLOOMING)	HEMP	SAGE (ARTEMISIA)	COMPOSITE	MISC.	PINE‡ (1933)	PLANTAIN	GRAND TOTAL
Amarillo, Texas	27	143	170	20	296	17	247	560	135	2		43	5	27			942
Atlanta, Ga.			3,310	94				52	68	2		8	35	29			3,504
†Boise, Idaho	24	185	209	35	82		63	145	46			153	8	34	139		595
Boston, Mass.			746	95				16	13				1	7			783
Brownsville, Texas			1,222	55				265	300	27		10	81	490			2,395
Buffalo, N. Y.			11,069	99				66	21			6	16	30			11,208
Charleston, S. C.			670	81				50	85				6	13			824
Chicago, Illinois	49	6,586	6,635	98				90	26				3	8			6,762
Cleveland, Ohio			6,306	99				80	22	3			5	14			6,430
Dallas, Texas			6,424	79				749	91	862		3	60	71			8,260
Denver, Colo.	775	1,657	2,432	40	1,336	176	778	2,290	112			613	40	61	759		5,548
Detroit, Mich.			6,779	99				62	7				3	7			6,858
Houston, Texas			7,255	97				27	96	75			25	27			7,505
Indianapolis, Ind.			18,405	98				163	120	1	5	22	11	33			18,760
Kansas City, Mo.	23	8,993	9,016	91				629	100	8	49	3	6	54			9,865
Knoxville, Tenn.			3,893	97				46	62	2		14	9	8			4,034
†Lander, Wyo.	1,258	75	1,333	44	122	78	173	373	202			965	9	141	785		3,023
Little Rock, Ark.			2,245	89				70	82	95			7	24			2,523
†Los Angeles, Calif.			144	37				102	50			8	2	82	22		388
Louisville, Ky.			7,339	95				143	85	5		76	9	24			7,681
Memphis, Tenn.			5,219	90				139	119	145		69	17	79			5,787
Mexico City, Mex.			34	11				40	97			1	19	121			312
†Miles City, Mont.	115	75	190	18	591		37	628	7			230	3	15			1,073
Milwaukee, Wis.	4	6,108	6,112	98				105	29			4	7	13			6,270
Minneapolis, Minn.	70	7,706	7,776	95				251	46			24	3	34			8,134
Mobile, Ala.			579	79				23	82				29	14			727
Montreal, Canada			899	97				9	7				2	8			925

TABLE III—CONT'D

	BURWEED MARSH ELDER	ALL OTHER RAGWEEDS	TOTAL RAGWEED	PER CENT OF GRAND TOTAL	RUSSIAN THISTLE	KOCHIA	MISC. CHENOPOD AMARANTH	TOTAL CHENOPOD AMARANTH	GRASS	ELM (FALL-BLOOMING)	HEMP	SAGE (ARTEMISIA)	COMPOSITE	MISC.	PINE‡ (1933)	PLANTAIN	GRAND TOTAL
Moorhead, Minn.	352	4,508	4,860	75	1,211	29	345	1,585	90		3	74	1	67	42		6,680
New Orleans, La.			3,183	85				50	128	3			329	21			3,714
New York, N. Y.			1,545	89				89	76				8	15			1,733
North Platte, Neb.	82	753	835	13	385	3,219	1,326	4,930	238			112	31	44	160		6,190
Oklahoma City, Okla.			5,395	62				2,333	362	81		58	66	51			8,346
Omaha, Neb.	587	8,794	9,381	73	161	169	1,438	1,768	186		1,236	5	2	160			12,738
Ottawa, Canada			583	82				72	23				28	16	2		722
Philadelphia, Pa.			2,841	97				47	19				3	10			2,920
†Phoenix, Arizona	20	125	145	11				808	248			2	19	67			1,289
*Pierre, S. D.	318	881	1,199	46	511	163	325	999	78			243	8	82	38		2,609
Pittsburgh, Pa.			4,652	98				29	10				11	10			4,712
Port Arthur, Canada			355	75	8		28	36	26			5	2	6	3	48	478
†Portland, Oregon			0	0	1		12	13	45					21	16	49	128
Raleigh, N. C.			1,715	95				33	51			3	3	14			1,819
†Reno, Nevada			12	3	150		33	183	40			48	19	72	972		374
†Roswell, N. M.	154	196	350	32	219		122	341	278			56	25	39	10		1,089
†Sacramento, Calif.			34	13	8		118	126	24			16		61	35		261
St. Louis, Mo.			9,956	94				439	73	5	9		8	25			10,515
†Salt Lake City, Utah	48	234	282	27	310	46	193	549	23			123	11	46	145		1,034
†Spokane, Wash.	1	7	8	3	68		77	145	31			21	4	42	291		251
Tampa, Fla.			554	68				19	123				34	86			816
*Tampico, Mex.			279	44				14	85			1	148	100			627
Toronto, Canada			1,534	97				17	16					10			1,577
Vicksburg, Miss.			1,820	82				61	65	196		22	14	48			2,226
Washington, D. C.			2,067	93				66	73				4	7			2,217
Wichita, Kansas			4,546	38				6,516	281	16		57	37	108			11,561
Winnipeg, Canada	38	469	507	65	177		107	284	11			18	13	19			852

*1932 Only.
†1933 Only.
‡Not included in totals.

the soil along the Atlantic Coast from Virginia around the Florida peninsula is not suited to the common ragweeds. The exact northern boundary of the ragweed area has not been determined, but the Great Lakes and the forested areas north of them seem to constitute an effectual barrier to both weeds and pollens. Further research will be necessary to learn just how far pollens are blown into eastern Canada. Lack of sufficient rainfall west of the hundredth meridian is the principal factor determining the western boundary of the ragweed area. While ragweeds are found throughout the western plains and the Rocky Mountain area, at no place west of central Kansas have excessive ragweed concentrations ever been found. In the Rocky Mountain area the ragweed problem is local rather than general. At

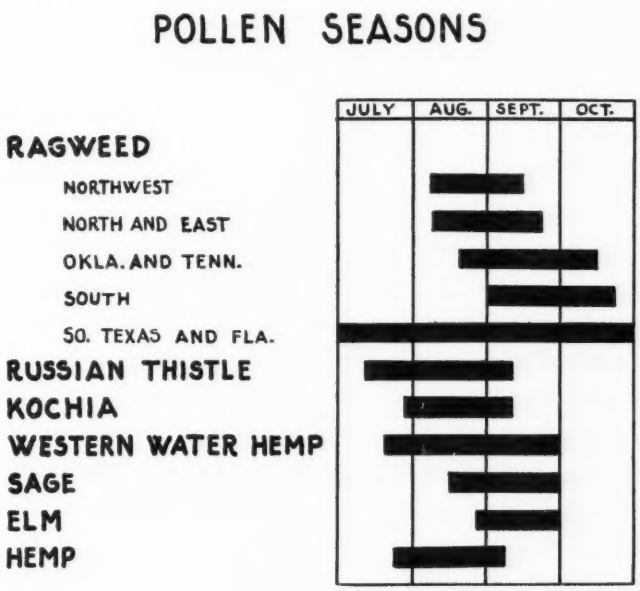

Fig. 2.—Approximate seasons of the more common summer and fall hay fever pollens.

Seattle and Portland, and presumably in the whole area west of the Cascades, no ragweed is found. Even at Spokane for the 1933 season only eight ragweed pollens were found on the slides during July, August, and September.

Without doubt most of the ragweed pollen in North America is produced by short ragweed (*Ambrosia elatior*) and giant ragweed (*Ambrosia trifida*). If the other ragweeds, burweed marsh elder (*Iva xanthifolia*) of the Northwest, southern ragweed (*Ambrosia bidentata*), and marsh elder (*Iva ciliata*) of the South, western ragweed (*Ambrosia psilostachya*), and the false ragweeds (*Franseria acanthicarpa*) of the West, and cocklebur (*Xanthium commune*) of agricultural states, were blotted out of existence, the national ragweed pollen crop would be only slightly diminished.

THE RAGWEED SEASON

While western ragweed and some species of false ragweed begin pollinating in the Southwest as early as May 15 (Fig. 2), the real ragweed season begins abruptly during the second week of August in the whole area east of the Rocky Mountains and north of Arkansas and Tennessee. In the southern states the onset of the season is from one to four weeks later than in the north. The pollen storm reaches its climax earliest in the high, dry region of the upper Missouri Valley about August 25—a week earlier than in the north half of the Mississippi Valley and the Great Lakes area. By the first week of September the center of the storm has begun to move southward,

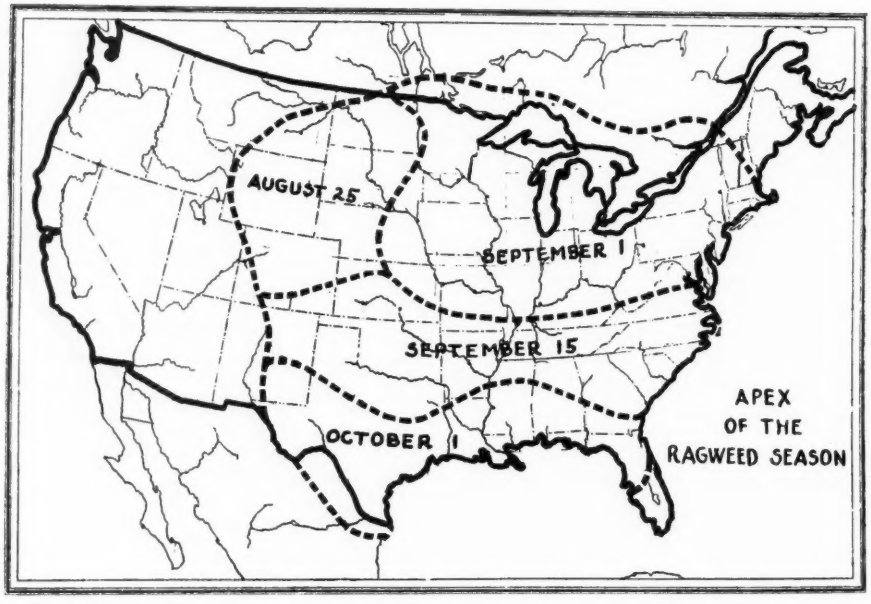

Fig. 3.—Maximum contamination of the air with ragweed pollen may occur several days earlier or later than the above dates, depending mostly on wind velocities during the season of maximum production.

reaching south Texas about October 1 (Fig. 3). The early approach of cool weather in the Dakotas, Montana and Wyoming limits heavy ragweed production to about thirty days. From forty-five to fifty days is the average length of the season in the central and southern states, with an extreme range of possible exposure of very sensitive hay fever sufferers in Brownsville, Texas, or southern Arizona of six months—May 15 to November 15.

Dates of onset, crises, and close of the season have been practically the same in most places each year except for the season of 1930, when the widespread drought was evidently the cause of considerable damage to giant ragweed. The onset of the season was about two

weeks later than usual, but the climax and termination of the season were typical.

The amount of ragweed pollen matured in a season varies considerably on account of the same factors that produce fluctuations in food crops. Due to the drought the yield in 1930 (Fig. 5) was only

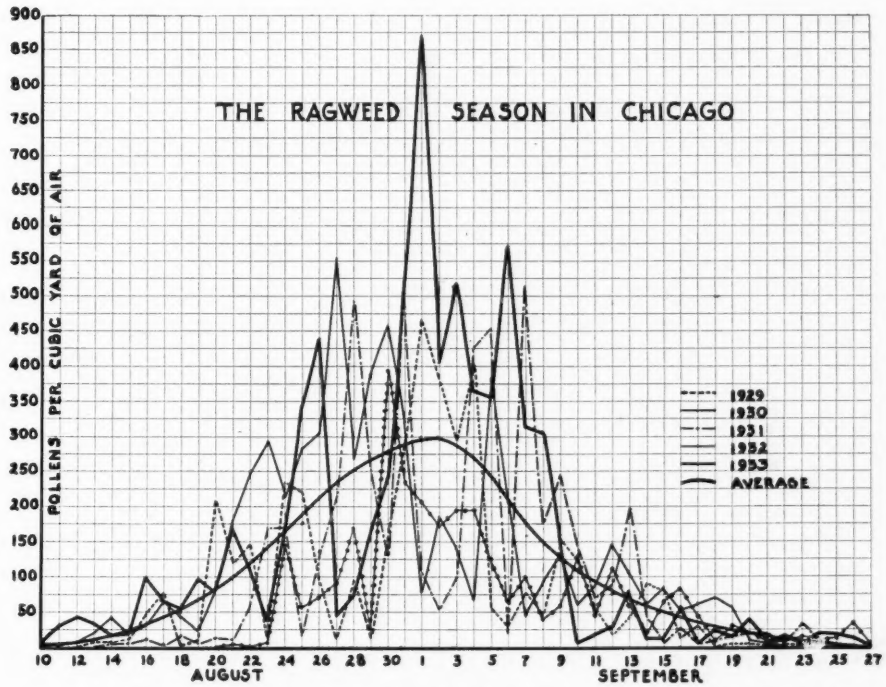

Fig. 4.—Five ragweed seasons in Chicago showing daily fluctuations and the five-year average. The fluctuations are greater in Chicago than in many other places on account of sudden drops due to pollen-free winds off Lake Michigan.

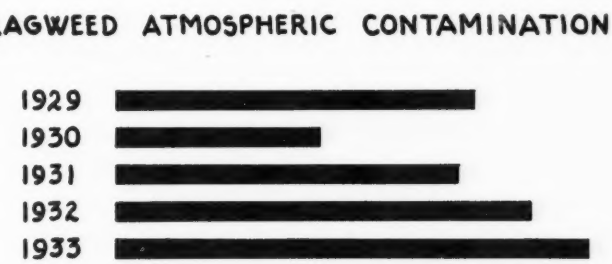

Fig. 5.—The average ragweed pollen crop for five years based upon the total amount found in 21 cities. This graph shows the short crop of 1930 due to the almost nation-wide drouth.

one-half that of the average for the other four years of the national study. In previous reports it was stated that the severity of the ragweed season seemed to depend upon the amount of rainfall during June and July. This index failed in 1933, when summer rainfall was only average, and the pollen crop the heaviest we have had. Heavy

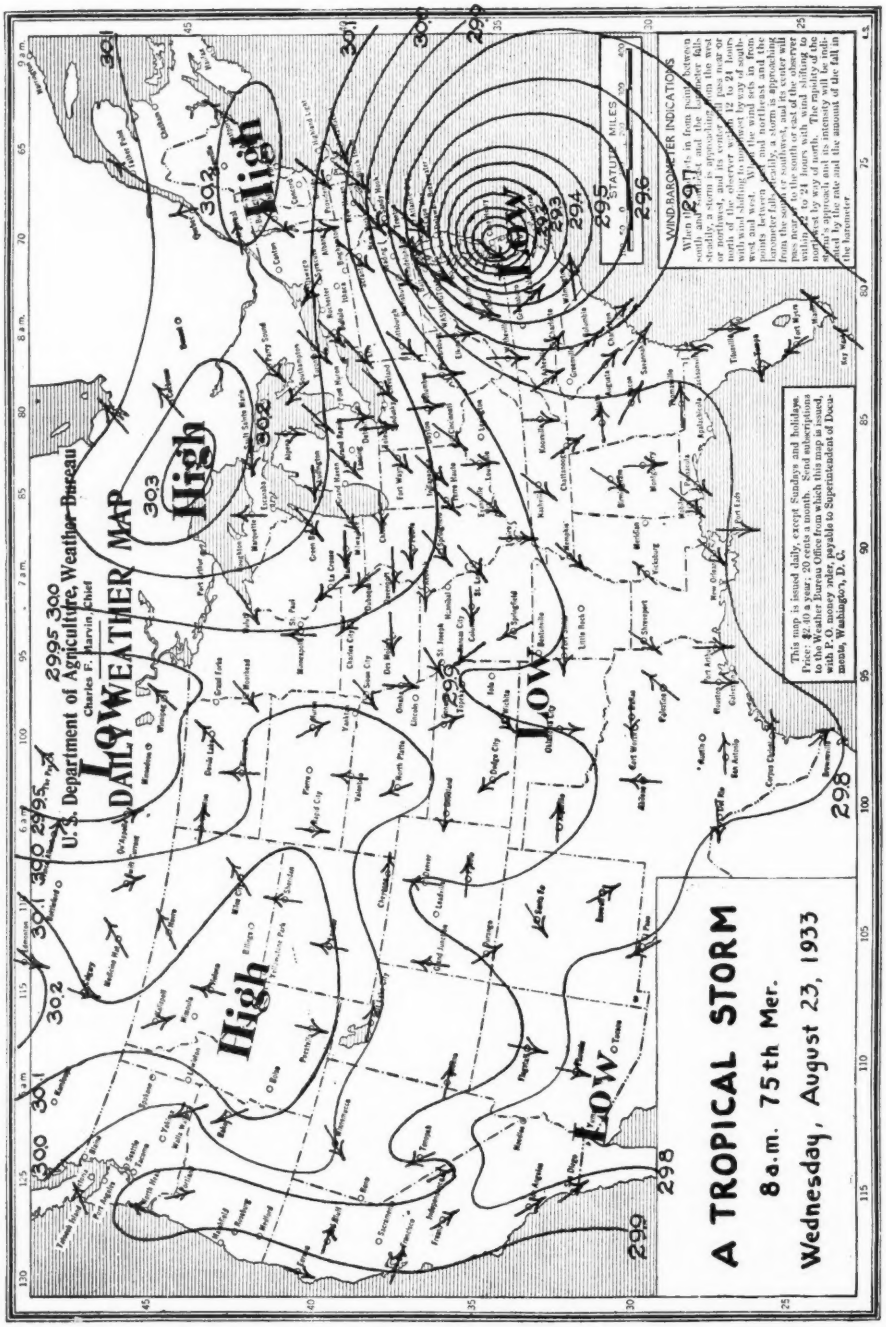

Fig. 6.—This map shows one stage in the progress of a typical tropical storm which swept northward along the Atlantic seaboard on August 22-24, 1933. Strong north winds across Ohio and Indiana carried unseasonable amounts of pollen as far south as Arkansas.

rains in May possibly account for the condition, as distribution factors (such as wind velocities and rainfall) in 1933 did not average better than in previous years. On the basis of pollen found on the slides, the total amount of ragweed pollen falling from the upper air in 1933 in the United States was not less than 275,000 tons.

The outstanding occurrence of the 1933 season was the wave of pollen blown southward from Indiana and Ohio almost to the Gulf on August 23 to 25 by the heavy winds caused by a tropical storm sweeping up the Atlantic Coast (Fig. 6).

TREE AND GRASS POLLENS

The tree and grass pollen records included in the tables and charts in this paper (except Table IV) are for the late summer and fall only, and do not cover the typical spring tree season and the adjacent grass season for early summer. These seasons have been studied intensively

TABLE IV

POLLEN CONTENT OF THE AIR. CHICAGO, 1933

MARCH TO MAY	PROPORTION FOUND
Hazel	2%
Maple (including box elder)	2%
Elm	8%
Oak	54%
Alder	2%
Pine	12%
Poplar	4%
Walnut and hickory	3%
Birch	2%
Grass	5%
Unidentified	6%
JUNE AND JULY	
Grass	63%
Pine	21%
Other trees	1%
Red sorrel	5%
Chenopod-Amaranth	1%
Unidentified	7%
AUGUST AND SEPTEMBER	
All ragweeds	98%
Burweed marsh elder (included in above)	1%
Chenopod-Amaranth	1%
MARCH TO SEPTEMBER	
Trees	12%
Grasses	4%
Ragweed	81%
Chenopod-Amaranth	1%

in only a few localities, and no extensive national data are yet available. Occasional grass pollens appear on slides throughout the summer and fall in all parts of the country, but only in the Central, West and South are the amounts great enough to be interesting. At Oklahoma City a maximum count of 40 grass pollens was found on one day during the second week of September.

Pine pollen, although regarded as unimportant in allergy, was noted in most western stations, especially at Reno, Denver, and Lander, Wyoming, during July. Attention has already been called to the local importance of scrub elm which pollinates during September in Texas. Small amounts of this pollen are sometimes found hundreds of miles east and north of the area in which it is produced.

THE CHENOPODS AND AMARANTHS

Of all weed families important in allergy, the *Chenopodiales* (chenopods and amaranths) are next in importance to ragweeds. Their active area lies west of the ninety-fifth meridian (approximate longitude of Kansas City). From central Kansas and Nebraska to Utah and Arizona, they often furnish more than one-half of all pollen found in the

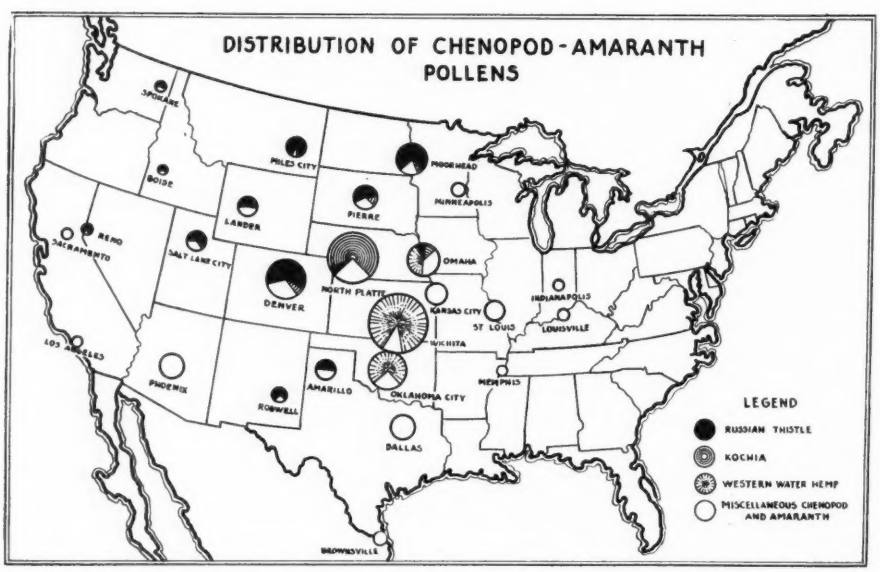

Fig. 7.—The relative area of the discs represents the proportionate totals of all chenopod-amaranth pollens found in the air in each city shown. The key indicates the proportion of pollen from the various species.

air during the summer and fall. In central Kansas and Oklahoma western water hemp often rivals ragweed in the abundance of pollen produced. It begins to pollinate at Wichita a month before the ragweed and continues through the ragweed season. This is a good example of a plant of prime importance but of restricted geographical distribution.

Russian thistle (*Salsola pestifer*) requires much less moisture than ragweed and is a formidable rival in the dry plains of the West and Northwest, and throughout the Rocky Mountain area. The eastern boundary of its active range is a line from western Minnesota, through western Texas, but its northern boundary in Canada is not yet determined. The largest records of Russian thistle come from Moor-

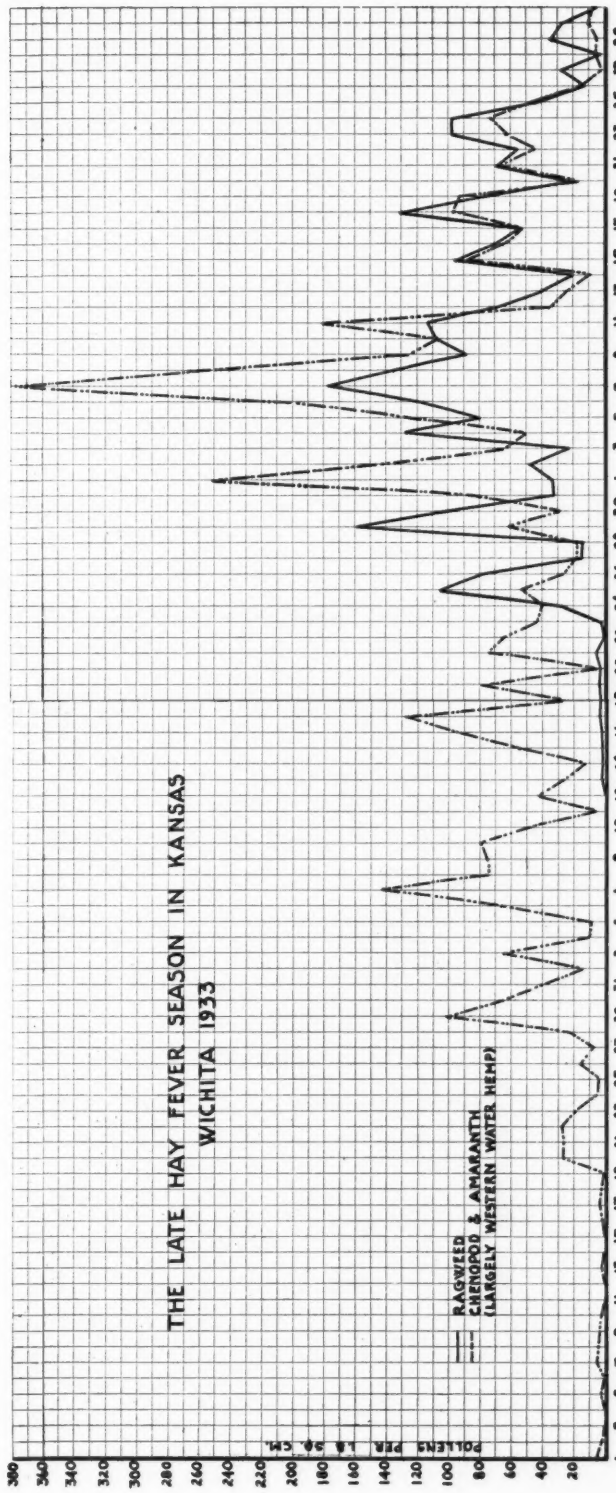

Fig. 8.—This graph shows the unusually long season of pollination of western water hemp. It will be seen that the ragweed curve follows the western water hemp curve, especially during the latter part of the ragweed season.

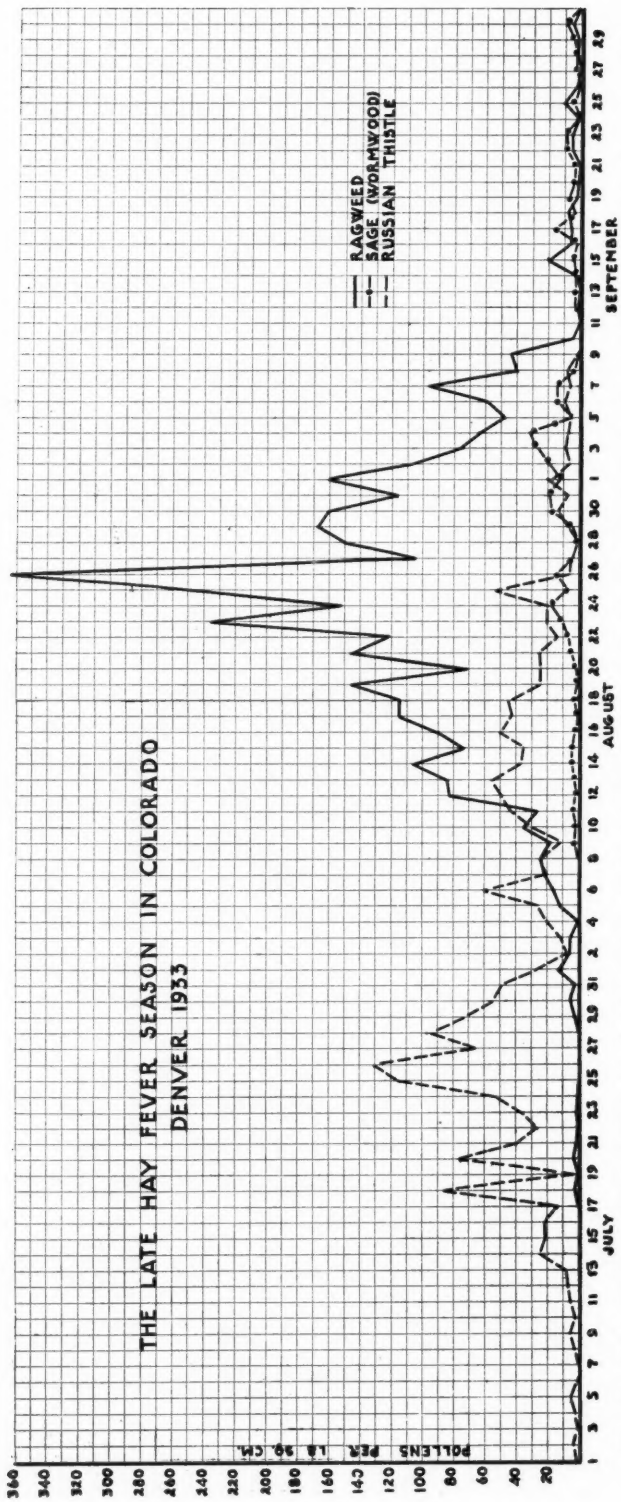

Fig. 9.—This graph shows the Russian thistle season beginning one month earlier than the ragweed season but lasting well into the ragweed season.

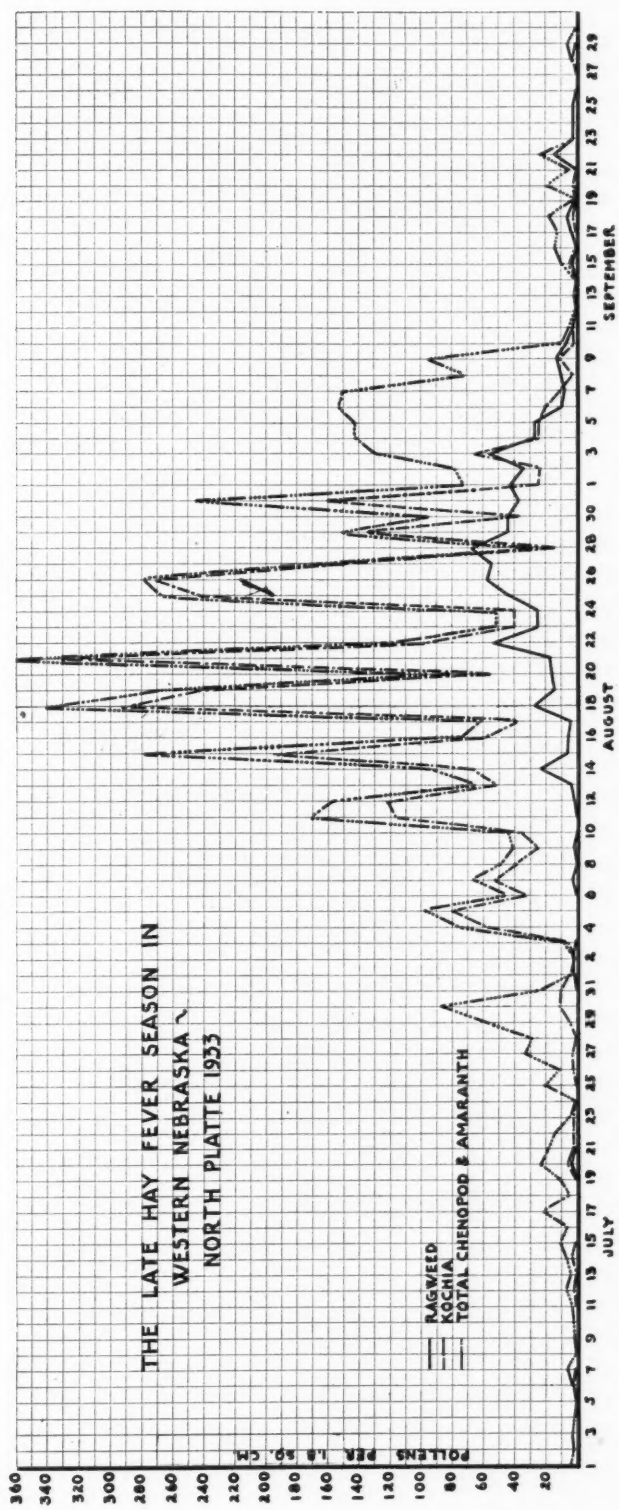

Fig. 10.—This graph shows the great predominance of kochia pollen at North Platte before and during the ragweed season.

head, Minn., and Denver, Colo., and the largest proportion at Pierre, S. D., and Miles City, Mont. The season lasts about two months, averaging from early July to early September.

Kochia *(Kochia scoparia)*, also called Mexican firebush, and summer cypress seems to be plentiful only in South Dakota, Nebraska, western Kansas, and eastern Colorado. Its season begins during the last week of July and closes during the second week of September. Kochia pollen is found in greatest amount and in greatest proportion at North Platte, Nebraska, where the slides catch almost four times as much of it as of ragweed pollen.

SAGEBRUSH AND RELATED SPECIES

Sagebrush *(Artemisia tridentata)* occurs throughout the Rocky Mountain area from Canada to Mexico, and related biennial species variously known as wormwood, mugwort, and sage are fairly common on the dry plains east of the mountains to central Nebraska. The active range of air-borne pollen from this genus seems to be the states of Idaho, Montana, Wyoming, Colorado, and the western parts of the Dakotas, Nebraska, and Kansas. The season varies considerably in different localities, but averages from August 15 to September 30. At Lander, Wyoming, sagebrush pollen is almost as abundant as ragweed, and the amount of this type of pollen at Denver is large enough to be of considerable importance.

COMPOSITES

Due partly to tenacious popular tradition and partly to careless selection and interpretation of skin tests, the pollens of the composite family, such as aster, daisy, goldenrod, dandelion, and similar plants, continue to claim an unwarranted share of attention. In the course

TABLE V

MAXIMUM POLLEN RECORDS

	MAXIMUM FOR 1 DAY	DATE	MAXIMUM FOR 1 YEAR	YEAR	CITY
Ragweed—short and giant	2,130	9/ 1/32	22,402	1933	Indianapolis, Ind.
Burweed marsh elder	184	8/19/33	1,258	1933	Lander, Wyo.
Russian thistle	185	8/21/33	2,007	1933	Moorhead, Minn.
Kochia	292	8/18/33	3,342	1933	North Platte, Neb.
Western water hemp	*900	8/29/32	*8,000	1932	Wichita, Kan.
Grass (fall species only)	40*	9/21/33	484	1933	Oklahoma City, Okla.
Plantain	53	8/24/33	96	1933	Port Arthur, Canada
Elm (fall-blooming species)	410	9/10/32	1,384	1932	Dallas, Texas
Hemp	128	8/15/33	1,554	1933	Omaha, Neb.
Sagebrush (and related artemisia)	117	9/15/33	965	1933	Lander, Wyo.
Composite	107	10/11/32	409	1932	New Orleans, La.

*Approximate.

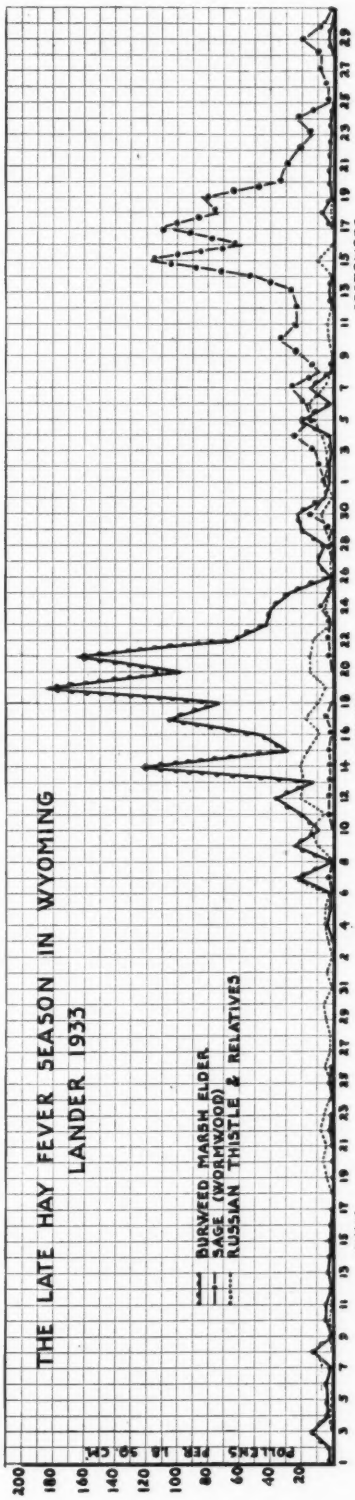

Fig. 11.—Most of the ragweed pollen found in the air at Lander, Wyo., was from burweed marsh elder. The sagebrush season occurs a month later than the ragweed season.

of this study goldenrod pollen has never been seen on the slides regularly exposed. In nine years' experience with over 16,000 slides, I have found a total of not more than 50 granules of goldenrod pollen, and most of these were found at one unusual ground level location. Only one granule of pollen from lettuce family has ever been noted. (This is the family to which dandelion belongs.) In all places in the United States the amount of composite pollen found during the season has always been less than 1 per cent, except at New Orleans. The source of the small composite pollens found usually in clumps on the New Orleans slides during September, and especially during October, has not been determined.

OTHER WEEDS

Hemp *(Cannabis)* pollen has been found on the slides in large amounts only at Omaha, Nebraska. The possibility of its being an important local factor elsewhere is great enough to warrant giving it a place in the "Rogue's gallery" of weeds.

English plantain (*Plantago lanceolata*), although usually regarded as a spring pollinator, is sometimes active in the fall. During the course of this study plantain pollen was found in interesting, although probably unimportant, amounts during July in Portland, Oregon, (probably the end of its season) and during August in Port Arthur, Ontario.

SUMMARY

1. A five-year study of ragweed pollen incidence in North America, involving more than 13,000 observations in 70 cities, is presented in condensed tabular and graphic form and briefly discussed.

2. A two-year study of all summer and fall pollens found in 60 cities of North America, is presented in condensed tabular and graphic form and briefly discussed.

CONCLUSIONS

The "gravity" method of collecting quantitative data on pollen incidence is simple and practicable, and yields valuable data from which to study the geographic distribution of hay fever plants, their pollinating habits, and seasons, and their relative importance in allergy.

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DISCUSSION OF "AIR STUDIES AT HIGHER ALTITUDES," BY ERNEST L. MACQUIDDY (PAGE 123), AND "THE POLLEN CONTENT OF THE AIR IN NORTH AMERICA," BY O. C. DURHAM (PAGE 128).

DR. MILTON B. COHEN, Cleveland.—Those of you who stay on the ground, I think, will have some difficulty in realizing the truth or the expectancy of the truth that Dr. MacQuiddy has been able to point out to us in the observations he has made at various altitudes.

I think that if his studies were made in this part of the country, where we have such tremendous quantities of fly ash and all sorts of smoke and pollen in the air, he would find he would collect all sorts of particles even higher than he does in his territory.

In my own flying experiences I have seen dust horizons over cities like Cleveland and some other industrial cities, 10,000 or 12,000 feet in the air. You can see a horizon as high as the cirrus clouds go, which is about 18,000 feet. You would get some of the things present at the ground level up there, because the cloud is a rising column of moist air which then preciptates moisture as the air cools.

I wonder, Dr. MacQuiddy, if the fact that you have more of the smaller things and less pollens, may not be due to the moisture being able to precipitate around the pollen particle, which is relatively large and comes down with the precipitation. Some of the other things being smaller occur somewhat higher. I know that as you fly around you can notice that wind velocities change tremendously at different altitudes and clouds move in various directions, and you would naturally expect that conditions would change almost momentarily from one place to another as you go along in an airplane.

That pollen travels tremendous distances cannot be doubted, because we have a number of patients in this part of the country who go to Canada seeking relief from hay fever. I have one physician who exposed plates on an island in Georgian Bay, 150 miles beyond any ragweed territory in Canada; and when there is a southwest or west wind, pollen will blow across from the Michigan peninsula, and he picks it up and his patients have symptoms.

DR. GEORGE PINESS, Los Angeles.—I should like to ask Dr. MacQuiddy whether the heights and altitudes mentioned in his paper were considered from the standpoint of sea level or altimetric readings from the airplane. Naturally if one were reading altimetric altitudes, one would not get the true idea of the height from which one is collecting pollen because it only reads from sea level.

I should like to ask Mr. Durham whether or not he purposely eliminated California and other areas from his chart. It seems to me that these areas are of equal importance in the study of the pollen contents of the air as those mentioned. It is true, however, that we are free of the ragweeds commonly found in the East. There is an abundance of western ragweed or *Ambrosia psilostachya*, but we have been unable to find the *Artemisia folia* or *trifida* that is so common in the East. There is a great abundance of amaranths and artemisias which he failed to mention in his paper. He makes light of the pollen problem of the Southwest, which in fact and truth is a very serious one since we are favored with an unusual variety and a large amount of pollen with practically a perennial season of pollination, meaning by this that there are flora of some kind or other pollinating throughout the year.

DR. HARRY S. BERNTON, Washington, D. C.—I am unable to discuss Dr. MacQuiddy's paper, but I want to thank Mr. Durham for his very valuable contribution to this field of work. I am glad he has been successful in securing the cooperation of the Department of Agriculture.

However, the clinical interpretation of these observations is another matter. A comparative study of pollen counts made in various sections of the country, during the ragweed season of 1929, is of interest. The atmosphere of New York had twice as many pollens as that of Boston, whereas Kansas City had 24 times as many—with a count of over 12,000 pollen grains. This mathematical index does not signify that the individual living in Kansas and suffering from hay fever has endured the maximum amount of distress. On the contrary, a patient living in the canyons of New York City may suffer just as intensely during the hay fever season, despite the fact that he does not see a blooming plant from morn to night.

It confirms the opinion that there is a minimal requirement of pollen for intoxication, and all in excess of that amount does not influence the course of the disease proportionately. That point should be borne in mind.

In addition to the quantity of pollen, the toxicity of the pollen is also of great importance. Botanists have noted that in some years the pollen grains are sterile. Whether that fact increases or decreases their toxicity, as far as hay fever is concerned, of course has not been determined, but it offers a very valuable field for investigation.

In Washington, for example, during this past spring, we have had a very severe tree pollination season. The patients with acute symptoms have been very sick indeed. The autumnal season of the year 1932 had been our worst to that date, but it has not been as bad as that of 1933; yet, in Chicago, 1933 proved to be very serious.

During these severe seasons, the hay fever patient of average sensitivity does suffer. The fact remains, however, that when the pollen content of the air shows a marked increase, new patients report to us who have never had the disease previously. When the tolerance of normal individuals is mightily overtaxed, new cases arise in which there is no positive family history of allergy.

The following point is also worthy of attention. A patient who receives in the course of prophylactic treatments allegedly 10,000, 20,000, or 30,000 pollen units does not necessarily acquire a greater tolerance than one who receives a much lower and more certain dosage.

DR. MACQUIDDY.—I should like to offer an explanation regarding hemp pollen to which Mr. Durham has called attention. This pollen being mostly found around Omaha and no other city, the explanation is that in about 1889 hemp was introduced there for the first time for the making of rope. It was introduced first at Fremont, Nebraska, later at Omaha, Lincoln and Columbus. We happen to be in the center of a lot of hemp which has grown wild from the fields which were planted there.

Mr. Durham also mentioned kochia. We have large quantities of this weed, but I have yet to see a patient who reacts to the kochia pollen. I wonder whether this is the experience of others.

Dr. Piness has raised the question concerning the altitude readings in my paper. I will state that the readings are those of the altimeter

and, in order to make them uniform with other readings that may be taken, 1,100 feet must be added, this being the elevation in and about Omaha, Nebraska.

Dr. Cohen brought up the question of dust particles. During the recent storms in Omaha I made some observations. The dust was carried up 10,000 feet and beyond, but my readings did not extend above the 10,000 foot level.

MR. O. C. DURHAM.—In giving this paper I fully realized that every man here who is treating hay fever knows more about his own local pollen problem than I do. The main purpose of this national study is to correlate local surveys and lay a solid foundation for comparative pollen studies. Every man has to work out his local problem for himself.

The question of quantitative amount is certainly interesting. There is no doubt there are many interesting local situations we have overlooked, and that there is plenty of pollen in Southern California to cause all kinds of hay fever, but from the first of July to the first of November there is not enough pollen in Los Angeles to contaminate the upper air the way we see it contaminated in the central states.

PATHOLOGY OF TWO FATAL CASES OF BRONCHIAL ASTHMA*

PAUL P. MICHAEL, M.D., AND ALBERT H. ROWE, M.D.
OAKLAND, CALIF.

IN 1922, Huber and Koessler[1] summarized and tabulated the histories, physical and pathologic findings of 15 cases of bronchial asthma then reported in the literature and of 6 additional cases of their own. In all these cases, the diagnosis was reasonably certain and autopsy reports included microscopic studies. In 1923, Lemierre, Léon-Kindberg and Lévesque[9] published macroscopic and microscopic observations on another case, and Rackemann[10] in 1926 published a similar record. Walzer[2] in 1930 republished the data assembled by Huber and Koessler and added 11 other cases from articles of Faschingbauer,[3] Dehner,[4] Kountz and Alexander,[5] Steinberg and Figley,[6] Bergstrand,[7] and Harkavy.[8] Since 1930, Clarke,[11] Wright,[12] Murphy and Case,[13] Fisher and Beck[14] have recorded single cases, and Macdonald[15] has added eight case and pathologic records. This makes a total of 49 records counting the two we are adding in this article, in which microscopic studies are described.

In 1926 Rackemann analyzed the case histories assembled by Huber and Koessler and concluded that patients 5, 7, 8, and 12 had died as a result of attacks of bronchial asthma. In two cases reported by Huber and Koessler the patients died during an asthmatic seizure. Lemierre, Rackemann, Clarke, Wright, Murphy and Case, Fisher and Beck, Steinberg and Figley added single case reports. Dehner and Harkavy added two reports, Kountz and Alexander added three and Macdonald added five. With the two records we are adding there will be 29 autopsy reports which include gross and microscopic pathologic findings on patients dying during attacks of bronchial asthma of the chronic type.

Death during attacks of bronchial asthma is not especially infrequent. In addition to the 29 cases already mentioned, Cabot[16] and Brown[17] have published gross pathologic findings on single cases. Case histories or records of death during attacks without pathologic findings have been reported by Rackemann in four instances, and recently in another case, a child by Bivings,[19] by Cohen and Rudolph[20] in five cases, and by Williamson[21] in two cases of pregnancy. Ratner[22] stated that he was "seeing more and more deaths in bronchial asthma resulting from morphine." Green[23] recently reported death due to asthma

*Read before the Twelfth Annual Meeting of the Association for the Study of Allergy, Cleveland, June 11, 1934.

in a pregnant woman. One of us (A.H.R.) observed death in two patients in addition to those we report, and from personal communications we have learned that most allergists have attended patients who have died during attacks of bronchial asthma.

CASE REPORTS

CASE 1.—A woman, aged forty-eight years, on moving from Canada to San Francisco seventeen years ago became susceptible to prolonged bronchial colds for three years. Then following tonsillectomy asthma developed and had persisted ever since except for a period of freedom for three weeks five years ago following a severe pneumonia. There had been no seasonal variation, and four to eight injections of adrenalin had been required daily for months. Nasal congestion without sneezing had been present since onset of asthma. No history existed of susceptibility to dusts, animal emanations, flowers or of food dislikes or disagreements. Aspirin and veronal produced asthma. Some abdominal distention and belching had been present for ten years. Constipation seemed to increase asthma. There was no history of hives, eczema, or headaches.

There was no history of asthma or any type of allergy in the family. Her periods were regular, not painful and recurred every twenty-two days for four days. She had had five intranasal operations. A double radical operation on antrums and ethmoids five years ago gave no relief. All her teeth had been extracted with no benefit to her asthma.

Her physical examination showed a thin, weak, constantly asthmatic woman weighing 94 pounds. Her skin was moist and moderately pigmented especially over exposed areas. Her hair was rather thin, slightly dry, and streaked with gray. Nasal passages were open and the mucous membrane was rather dry. Tonsils and teeth were all out. There was a slight diffuse granular enlargement in the right lobe of the thyroid. Chest was emphysematous and thin. Typical asthmatic wheezing and breath sounds were heard throughout both lungs. The heart was not enlarged to percussion. The sounds were regular, of fair quality, with no murmurs. Pulse was 100. Radials and other peripheral vessels were not sclerotic or tortuous. Blood pressure was 160/110. The abdomen was negative. Pelvic examination was negative. The extremities and reflexes were also negative.

Roentgen ray film of chest showed a number of calcified glands in each hilus with increased bronchial markings especially in the lower right lobe. Films of sinuses showed opaque antrums (due to radical operations?) and a small slight gray sphenoid.

The urine analysis was negative. Red blood count was 5,180,000 with a hemoglobin of 99 per cent; the white count was 10,200; the differential showed 70 per cent polymorphonuclears, 18 per cent lymphocytes, 8 per cent eosinophiles, 4 per cent large mononuclears. The

Kahn reaction on the blood serum was negative. Serum proteins were albumin 5.15, globulin 2.02.

Skin reactions by the scratch method showed no definite reactions to any food, animal emanation, miscellaneous, pollen or dust allergens except to 3 stock house dust extracts. Intradermally the patient gave a 2-plus reaction to rabbit hair and *Franseria bipinnatifa* and a one-plus reaction to *Chenopodium album.*

The patient was given various elimination diets and lived in rooms in which the environment was carefully controlled. She was hyposensitized with pollen, and dust extracts and very small and increasing doses of vaccine prepared from her sputum and stool were administered intradermally and subcutaneously. Peptone hypodermically, large doses of dilute HCl by mouth, potassium iodide and nitrate by mouth and neosalvarsan by vein gave no help. No morphine sulphate

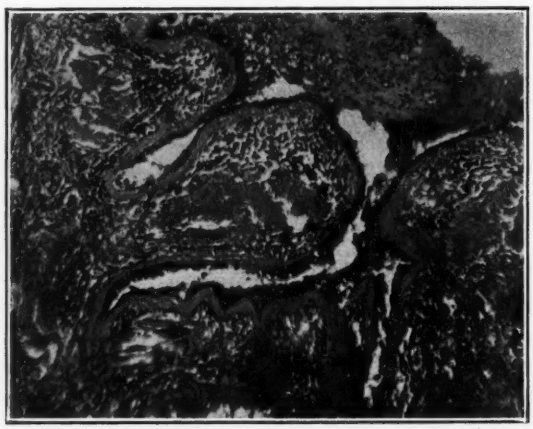

Fig. 1.—(Magnification 300 times.) Section through a 4-6 mm. bronchus. Note the thick bronchial exudate consisting of coagulated fibrin, mucus, lymphocytes, and eosinophilic cells. The mucosa is intact but the basement membrane is markedly hypertrophied. Eosinophilic cells form a large percentage of cells both in the lumen and in the tissues.

was ever given although codeine was administered with some relief to her coughing. Finally, in October, she became worse and very weak. She came to the hospital into an air-conditioned room, and died suddenly, having had 7 doses of adrenalin during the night. The nurse had spoken with her five minutes before her death and her pulse and respiration had both stopped when she was next seen. Three hours later an autopsy was performed by Dr. Paul Michael, pathologist to the Peralta Hospital.

Autopsy Findings.—Inspection: The subject appeared in a fair state of nutrition and development, well within the age limit of forty-nine years. Rigor mortis and postmortem lividity were present in the early stages. The chest appeared somewhat emphysematous (barrel shaped), but otherwise there were no important or remarkable changes noted. Weight about 115 pounds; 5 ft. 2 in.

The usual midline incision was made and a small amount of subcutaneous fat was encountered. The abdominal cavity exhibited a normal gastrointestinal system, a not unusual pelvis, a somewhat congested liver and spleen, a normal pancreas. Both kidneys were of normal color, shape and consistency, and the adrenal glands appeared somewhat edematous. The bladder and ureters showed no pathologic condition.

Upon opening the thoracic cavity, the lungs ballooned out into the exposed field. They appeared somewhat congested, emphysematous, with some few small scattered patches of atelectasis at the base anteriorly. This entire atelectasis covered an area approximately 4 cm. square. The heart appeared of normal size and shape. None of the cavities were distended or dilated, and the auricular and ventricular walls were of normal thickness. The endocardium and pericardium

Fig. 2.—(Magnification 300 times.) Section of 4-6 mm. bronchus showing infolding, hypertrophy of basement membrane, and definite layers of the bronchial exudate.

appeared smooth throughout. The color of the heart musculature was somewhat pale and the consistency less firm than normal. The aorta showed normal measurements. Examination of the thymus revealed some enlargement (6 gm.), and cut section showed a definite lymphoid hyperplasia. There was no evidence of pleural adhesions or any type of chronic pleuritis.

The lungs appeared somewhat voluminous upon removal, and weighed 360 and 346 grams, right and left respectively. Upon pressure they gave an emphysematous sensation. Bronchial glands were everywhere enlarged, hyperplastic and somewhat anthracotic and ranged in diameter from 3 mm. to 1 cm. Upon opening and tracing out the branches of the left and right bronchial tree, fairly large gelatinous plugs were observed obstructing the lumina of many of the middle-sized and intermediate bronchi. In many instances this exudate was closely adherent to the mucosal lining. The bronchial muscle

layer appeared thickened and the soft tissues surrounding the bronchi infiltrated by a cellular exudate. Upon removing the tenacious exudate from the bronchial walls, the underlying mucosa appeared hemorrhagic and congested. This congestion also extended up into the larger bronchi and into the trachea.

Microscopic Findings.—Adrenals: The adrenal tissue showed atrophy of both cortical and medullary zones. Associated with edema of the cells, however, was a small degree of interstitial edema. Vascular channels appeared engorged and dilated with blood. In several areas of the adrenals were groups of eosinophilic cells of the polymorphonuclear and mononuclear varieties. What was thought to be enlargement of these glands on gross examination turned out on microscopic sectioning to be an actual atrophy of the parenchymatous cells with hypoplasia, but with a supplanted cellular invasion and serum engorgement. Vessel walls in the adrenal tissue did not appear thickened or sclerosed.

Heart: The heart muscle presented a very mild degeneration but no evidence of hypertrophy, interstitial fibrosis, fatty degeneration or infiltration. The coronary vessels were thin-walled and showed no evidence of sclerosis or calcification. The aorta was within normal microscopic limits. The endocardium presented no pathologic changes.

Thymus: The thymus gland was the seat of a marked lymphoid hyperplasia. There was a mild degree of interstitial edema, with degenerative changes of the fibrous tissue stroma. There was no infiltration of the tissue by eosinophiles.

Lymph nodes: The lymph nodes noted to be enlarged grossly presented microscopically a diffuse hyperplasia, with many active germinal centers. Lymph follicles were numerous. There was a small increase in fibrous tissue observed, especially associated with the many anthracotic areas present in the nodes. There was no evidence of eosinophilic invasion or healed tuberculosis.

Spleen and Liver: Both the spleen and the liver appeared the site of a mild chronic passive congestion. The spleen appeared rich in eosinophilic cells, especially in the pulp. Lymphoid elements were not numerous in the spleen. The liver presented a mild cellular reaction, with small scattered groups of mononuclear eosinophilic cells in the perivascular spaces. Blood vessels were not thickened.

Lungs: The atelectatic patches, described grossly, revealed compression of the alveolar walls resulting in obliteration of the alveolar cavities. There was some hemorrhagic infiltration of the tissue in the alveoli. In many of the areas surrounding the bronchi there was some increase in fibrous tissue with compression of the alveoli. These areas appeared in the form of collars and extended outward for a distance of 5 to 15 mm. Cellular infiltration consisted chiefly of mononuclear eosinophiles.

Bronchi: (A) 8-10 mm. bronchi: These bronchi appeared definitely thicker than normal with increased thickness of the walls as well. The epithelium was of the flattened type, partially disintegrated, and the mucosa showed only hyaline changes. The exudate in the lumen was more mucoid and less cellular and with less apparent evidence of adherence to the epithelium. There was no evidence of cellular infiltration of the wall breaking through the mucosa into the lumen. Glands were numerous and hyperplastic, and there was a dense cellular exudate in the peribronchial area. Lymphocytes particularly preponderated in the exudate, although mononuclear eosinophilic cells also were seen. The bronchial muscles appeared moderately hypertrophied and showed some vacuolar degeneration.

Bronchi: (B) 6-8 mm. bronchi: The total thickness through the wall of these bronchi was increased over the normal. The muscle

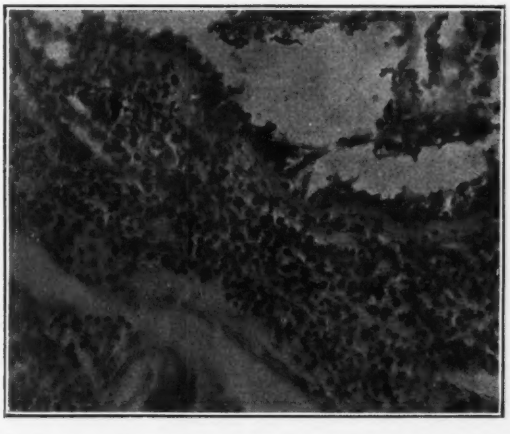

Fig. 3.—(Magnification 700 times.) High power view of membrane showing submucosal cellular invasion. Eosinophilic cells show a differential count of 95 per cent. (4-6 mm. bronchus.)

showed definite hypertrophy and degenerative changes with myositis existing. The epithelium was flattened but apparently intact; hypertrophy and hyalinization of the basement membrane were present, and infolding or sacculation of the mucosa was greater than in the 8 to 10 mm. bronchi. The exudate showed definite lamination, was mucoid with a larger number of cells present than in the larger bronchi. The infiltration consisted of endothelial macrophages, lymphocytes, and fairly numerous eosinophilic cells. The glands in the wall were hyperplastic and in some areas disintegrated and frequently were infiltrated by inflammatory lymphocytes and eosinophilic cells. The cartilage did not appear to be disintegrated. There was, however, an increased fibrosis surrounding these bronchi.

Bronchi: (C) 4-6 mm. bronchi: These bronchi tended to be collapsed and showed marked infolding and sacculation of the mucosa

with thickening and hyalinization of the basement membrane with decrease in elastic tissue. The epithelium was disintegrated in many areas and essentially was of the flattened type. The exudate in the wall appeared to have broken through the mucosa in some areas and extended into the lumen of the bronchi. The muscle showed a myositis with vacuolar degeneration and cellular infiltration with partial destruction by lymphocytes and eosinophilic cells. The subepithelial layer was thickened, was infiltrated by inflammatory cells of all varieties with a moderate interstitial fibrosis. In comparison to several normal lungs as controls, the degree of infolding of the mucous membrane was definitely increased over the normal as well as the hyalinization and hypertrophy of the basement membrane. The muscle thickness also was increased over the normal lungs.

Bronchi: (D) 2-4 mm. bronchi: These bronchi showed a moderate collapse with definite infolding of the bronchial mucosa, thinning of the epithelium and hypertrophy with hyalinization of the basement membrane. The elastic tissue was decreased in amount. The exudate in the lumen was laminated with a large amount of fibrin and mucus and fewer numbers of cells than seen in the 4 to 6 mm. bronchi. There were numerous red blood cells, however, seen in this sized bronchus. The exudate was rich in macrophages and lymphocytes. The few muscle fibers showed degenerative changes and some slight hypertrophy.

Bronchi: (E) 2 mm. and less bronchi: These bronchi showed two distinct pictures; some were the seat of dilation, lined by a flattened epithelium and showing no infolding or hypertrophy of the basement membrane. These bronchi were also essentially devoid of any exudate. The surrounding alveoli showed compression and marked congestion with some fibrosis. The other bronchi of this size showed definite infolding of the mucosa with hyalinization and hypertrophy of the basement membrane. The interesting feature was that in these bronchi there was the same general type of collapse, but the muscle was either absent or sparse. Probably causation of the infolding was due to scarring and contracture of the wall due to changes seen in the basement membrane. There was a cellular and fibrinous exudate seen in the lumina, and the surrounding tissues were compressed and somewhat fibrous. The vessels were markedly congested.

Case 2.—A woman, aged fifty-seven years, had had hay fever during the spring, summer and fall for sixteen years until bronchial asthma developed four years ago in October. During the first year there was much coughing and irritation of the throat with gradually increasing expectoration. Since September three years ago, severe asthma had been practically constant. For the last four months, she had followed a diet of fruits and vegetables given by a chiropractor with a weight

reduction from 135 to 108 pounds. For several months spasmodic asthma with little ability to expectorate had occurred, and two months ago she was so distressed that she was unconscious for several hours. Flowers had never bothered her. Dust made her sneeze, but she had never noticed any nasal or bronchial symptoms from animal emanations. No definite food idiosyncrasies were known, and she had never had any headaches, unusual gastrointestinal symptoms and no hives or eczema. The mother had coughed all her life. A brother had bronchial asthma. No previous history of colds or coughs, or of illnesses. All upper teeth were extracted twenty-five years before and the lowers four years ago. Her periods had stopped when she was forty-eight years old. She had had no operations on her nose or sinuses.

Physical examination revealed a thin, poorly nourished woman having severe spasmodic asthma. The skin was dry. Eyes were negative. Her nose was not occluded although the membrane was pale, moist

Fig. 4.—(Magnification 500 times.) Section taken through the muscle of a bronchus, showing a definite myositis with cellular infiltration, degeneration of fibers, and increased vascularity.

and moderately edematous. There was no adenopathy but a small enlargement in the left lobe of the thyroid. The teeth were false. Tonsils were flat. Chest was thin and moderately emphysematous. Shoulders were high and respiratory excursion was slight. The lungs showed diffuse signs of bronchial asthma in all parts. The heart was small to percussion. Sounds were of fair quality, regular with no murmurs. Blood pressure was 140/90. No organs or masses were felt in the abdomen. Pelvic examination showed a small uterus. Extremities and reflexes were negative.

Roentgen ray film of chest showed definite emphysema with a moderate increase in the shadows in each hilus and increased peribronchial markings throughout the inner and middle thirds of each lung. Films of the sinuses showed a moderate swelling of the membranes in each antrum.

Urine analysis was negative. Blood count showed hemoglobin 86 per cent; red blood count 4,780,000; white blood count 12,550; and a differential count of 68 per cent polymorphonuclears, 16 per cent lymphocytes, 10 per cent large mononuclears, and 6 per cent eosinophiles.

Skin tests by the scratch method showed no reactions to food, animal emanation, grass, tree, dust, or miscellaneous allergens but large reactions to all *artemesia* pollens and definite reactions to chrysanthemum and dahlia pollens. Intradermal reactions were obtained to chicken feather, dog hair, horse dander, and wool allergens and to ray grass, bermuda grass, rough pigweed, spearscale, pickle weed, Russian thistle, western ragweed, cosmos, coreopsis, and live oak pollens.

Since her history and skin reactions pointed to a pollen asthma, desensitization was attempted with antigens containing all important pollens to which the patient reacted. Air-conditioned, pollen-free rooms were used for several weeks. In spite of continued therapy, her symptoms were little relieved even during several weeks of rainy weather when practically no pollen was in the air. In addition, various elimination diets were tried. She was given potassium iodide, nonspecific protein therapy and neosalvarsan. Autogenous vaccines were given in minute and later in larger doses with no help. Finally in October of our second year of attempted control, her asthma became more intractable, the breathing more difficult, and her ability to raise any mucus practically lacking. Bronchoscopy was thought of but her weakness contraindicated it. Finally during one of her severe paroxysms she died, apparently from suffocation. No morphine was administered, but large doses of adrenalin had been given many times a day for many months.

Autopsy Findings.—Inspection: The body was that of a female of about the stated age of fifty-five years, appearing markedly emaciated. Bones, joints, and other fixed points were markedly prominent. Eyes showed many small petechial hemorrhages, probably resulting during the final attack. Ears and nose grossly negative. Mouth, upper and lower plates were present. Right antrum was opened and portions of bone and sinus membrane were removed. They appeared very white, pale and avascular. Over the arm were many small needle points from previous injections of adrenalin. There were no other marks of identification or abnormalities. The body weighed approximately 85 pounds and was approximately 5 feet 2 inches in height. Rigor mortis and postmortem lividity were present. Autopsy was done eight hours after death.

The usual midline central incision was made, and an extremely small amount of subcutaneous fat was encountered. The thoracic and abdominal cavities were examined and contents inspected in situ. The abdominal cavity exhibited no gross abnormalities.

Gastrointestinal system was examined throughout and found to be negative.

Upon opening the thoracic cavity, both lungs appeared extremely voluminous and crepitant. Upon making a slit into the left lung, a bloody material exuded. There were some old adhesions near both bases, although these were not prominent. Diaphragm on both sides appeared depressed, especially on the right side, approximately 2 cm. below the normal level. The right lung was removed and weighed 334 grams. It was very emphysematous, and at the base many small purulent petechial hemorrhages were seen. Anthracosis was present throughout. There were no areas of atelectasis seen. The lungs appeared slightly gray in color, and they appeared slightly hyperemic near the bases. At the hilus there were many enlarged darkly colored lymph nodes seen. These appeared situated around the bronchi and

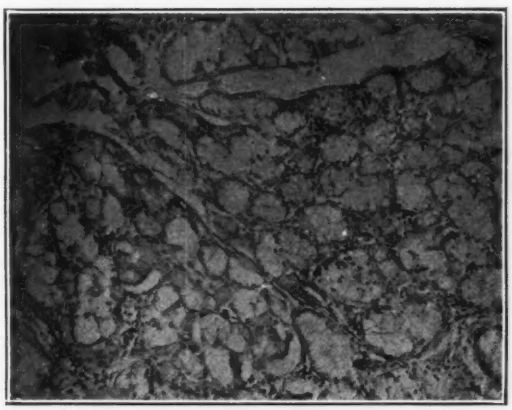

Fig. 5.—(Magnification 300 times.) Section showing hyperplasia of bronchial glands with increased activity and increased vascularity, accompanied by eosinophilic invasion. (4-6 mm. bronchus.)

apparently caused some obstruction due to pressure. The bronchi throughout appeared to have thickened walls and they appeared definitely dilated. In the right plexus at the bifurcation, there was a mucopurulent exudate which was seen to continue on down through the right lung into the terminal bronchi. Very little air space could be observed within the bronchi of this right lung. This exudate was thick and tenacious. It was fairly adherent to the bronchial mucosa and appeared very elastic. The right lung throughout was hyperemic and congested and diffusely emphysematous. The left lung showed some old pleural adhesions near the base and in this same area were many small petechial subpleural hemorrhages. It was diffusely emphysematous, slightly gray in color. Medium-sized bronchi all showed almost complete occlusion, due to the same type of mucoid exudate. This appeared laminated, very elastic, and was fairly adherent to the mucous surface of the bronchi. The surrounding bronchial tissue ap-

peared very cellular and congested. Bronchial lymph nodes, especially in the hilum, were dark in color, very densely cellular and markedly enlarged. They caused definite partial obstruction to the bronchi.

The heart was small, weighed 200 grams, had a very firm musculature throughout, presented a normal color and shape and had a very firm consistency. Coronary vessels were soft and pliable and showed no occlusion or obstruction. The right auricle was within normal limits. Tricuspid valve measured 12.8 cm. The right ventricle showed a fairly firm musculature and no dilatation. The left auricle showed no gross abnormalities and the endocardium was normal. The mitral valve ring was elastic and measured 9.7 cm. The pulmonary and aortic valves were normal and the coronary orifices were patent. Cardiovascular system was examined throughout and there was no sclerosis seen.

Fig. 6.—(Magnification 300 times.) Noncollapsed 2 mm. bronchi from an asthmatic lung. There is practically no exudate within the bronchi, there is no hypertrophy of the basement membrane and no infolding of the mucosa is seen. These bronchi are distal to the bronchi where the pathologic changes were most marked.

The aorta appeared extremely small but was elastic and showed no sclerosis or degeneration.

The liver appeared moderately enlarged, very firm in consistency, and showed no evidence of stasis or degeneration.

The pancreas was within normal gross limits.

Both adrenals appeared quite congested, very cellular and hyperemic, and densely yellow in color.

The thymus was removed and weighed 7 grams. It appeared quite densely cellular and fairly firm in consistency.

Kidneys weighed 115 grams respectively. They were small, had smooth surfaces, and the capsules stripped easily. Cut section showed normal thickening throughout. Both ureters and bladder were normal.

The ampulla of Vater was patent, and bile could be expressed by pressure on the gallbladder.

The spleen was small, weighed 90 grams, was firm, densely cellular and not congested.

The uterus was small and infantile in type, had a thin wall and an atrophic endometrium.

Both tubes were small and the ovaries extremely atrophic.

Lymph nodes apart from those near the bronchi were not remarkable.

Diagnosis: Bronchial asthma; pulmonary emphysema; hyperplastic lymphadenitis; hyperplastic thymus; hypoplasia of aorta.

Microscopic Findings: The microscopic sections through the lungs showed some areas of emphysema with thin-walled air vesicles which were dilated. These emphysematous areas appeared to be on the peripheral parts of the lung particularly. There was no cellular infiltration seen in these areas. In the region of the larger bronchi and the medium-sized bronchi, the lungs showed marked cellular infiltration, especially surrounding the bronchial mucosa out into the musculature of the bronchi and into the surrounding lung tissue; in the region of the larger bronchi there were many hyperplastic areas of lymphoid tissue seen with degeneration and some eosinophilic infiltration. The same lymph nodes had lost their normal structure, and the lymphoid follicles were no longer visible. There was also some old changed blood pigment seen in the medullary portions of these small nodes. The mucosa of the bronchi, both large and medium size, and even some of the smaller ones, showed marked disintegrated cells, fibrin, and tissue débris. The epithelium itself was about one-fifth normal thickness resulting from disintegration. The basement membrane was tremendously hypertrophied, about five times over normal and showed hyaline degeneration. Cellular infiltration extended from the basement membrane out into the surrounding tissues involving the muscle layer, glands, and even some of the cartilage. The muscle tissue was definitely degenerated, pale staining, and also showed hypertrophy. The glands were all hyperplastic and showed some cellular infiltration. Differential count of cells showed some eosinophilic cells forming approximately 25 per cent.

Bronchi: (A) 10-8 mm. bronchi: Same findings as in Case 1. Lymphocytic cellular infiltrate in wall of bronchus, with fairly dense infiltrate in the peribronchial tissues. Exudate in lumen was less cellular than in smaller bronchi.

(B) 8-6 mm. bronchi: Hypertrophy of bronchial muscle was in evidence, with some myositis. Exudate in lumen was more cellular than in larger bronchi. Epithelium flattened.

(C) 6-4 mm. bronchi: Exudate was adherent to the epithelium, which was flattened, with areas occasionally of complete disintegration of mucosa, allowing cells to fill the lumen. Exudate was layered. There was muscle hypertrophy with myositis. The basement membrane was degenerated, with hyaline changes. Epithelium and mucosa

were infolded. Total diameter was increased in all bronchi of this size. Eosinophilic cells predominated both in lumen, wall, muscle, and in surrounding tissues.

(D) 4-2 mm. bronchi: Changes same as in Case 1. Bronchi were partially collapsed, with infolding of mucosa, similar type of exudate as noted in Case 1. Myositis was present.

(E) 2 mm. and less bronchi. Many were collapsed, with infolding of mucosa, hyaline degeneration of basement membrane, and cellular exudate in lumen. Other bronchi were widely dilated, with no hypertrophy of basement membrane. Epithelium was flattened. Mild atelectasis of surrounding alveoli was present.

The thymus showed some hyperplasia, increased cellularity, but otherwise nothing unusual was observed. There was no eosinophilic cellular increase in the thymus.

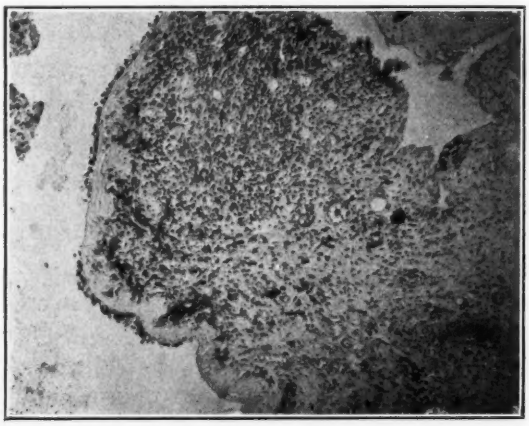

Fig. 7.—(Magnification 300 times.) Taken from sinus membrane of Case 2. (Right antrum.) There is thinning of epithelium, with hypertrophy of basement membrane, and a dense cellular exudate with large numbers of eosinophilic cells. The differential count of these latter cells is approximately 65 per cent.

Heart: The heart showed essentially normal findings with no apparent hypertrophy fragmentation or degenerative changes seen in the fibers, and coronary vessels were thin walled and there was no evidence of any sclerosis or unusual calcification. Pulmonary vessels were normal.

Maxillary Sinuses: The epithelium in some areas was the high columnar type with some cilia. Generally, the epithelium was flattened and rested upon a markedly thickened and hyalinized basement membrane. The sinus membrane was thrown into folds and was definitely thickened and edematous. There was a zone of cellular infiltration seen extending from the basement membrane down to the periosteal layer. The capillaries were moderately engorged, and there were some perivascular collars of round cells. The differential count of the cells seen in the

sinus membrane showed approximately 65 per cent mononuclear and polynuclear eosinophilic cells.

The liver showed no microscopic changes.

Adrenals were moderately congested, fairly deeply staining, and showed a few eosinophilic cells, both cortical and medullary layers.

The kidneys showed no microscopic changes.

The gallbladder was negative.

The spleen showed no microscopic abnormalities.

Sections through the aorta showed some thickening, but no areas of degeneration, sclerosis or cellular infiltration.

COMMENT

The macroscopic and microscopic findings in our patients coincide in the main with those reported by Huber and Koessler, and Kountz and Alexander, Macdonald, Harkavy, Fisher and Wright in emphasizing the frequency of the following findings in patients dying during attacks of bronchial asthma. These findings have recently been summarized by Steinberg. Macroscopically there is varying emphysema, increased thickness of the walls of bronchi with a narrowing of their lumina, an increased thickness and infolding of the mucous membrane, excessive mucus or the presence of plugs of tenacious mucus and fibrin in most bronchi and some dilatation of smaller bronchioles and alveoli. Microscopically there is the increased thickness and infolding of the mucous membrane of bronchi larger than 2 mm. to 3 mm., and infiltration of the mucosa, submucosa, mucous glands and even the muscles and at times the cartilage with eosinophiles, plasma cells and lymphocytes, a thickening and hyalin degeneration of the basement membrane which Macdonald states is the most important finding and a hypertrophy of the muscles. The increased thickness of the bronchial walls was shown by the careful measurements of Huber and Koessler and corroborated through the careful studies of Kountz and Alexander. The narrowing of the bronchi was especially demonstrated by Wright's case in which the bronchi after their second bifurcation were nearly completely occluded due to thickening of the walls. What was apparently described by most of the authors but not considered as such was a myositis of the bronchial muscle. This myositis observed in our cases was seen in the degenerative changes and the cellular invasion which appeared to be as prominent as the hypertrophy.

Walzer[2] in a careful analysis of available findings up to 1931 concluded there was no characteristic picture in bronchial asthma and that the thickening of mucosa and basement membrane and the hypertrophy muscle could result from secondary bronchitis and emphysema. His summary of the various pathologic findings on page 164 of his book is carefully compiled. However, since Walzer's discussion Macdonald, Wright, Fisher and Murphy have reported further autopsies

which emphasize the picture as outlined by Huber and Koessler and Kountz and Alexander, and our 2 cases again indicate the occurrence of a characteristic pathologic condition as summarized in the preceding paragraph.

CHART 1

SUMMARY OF PATHOLOGIC FINDINGS IN BRONCHI

SIZE	CASE 1	CASE 2
A. 10-8 mm.	Moderate dilatation, mild infolding of basement membrane; moderate hypertrophy and hyalinization of basement membrane. Exudate more mucoid, less cellular. Muscle shows mild degeneration and hypertrophy.	Same findings as in Case 1. Lymphocytic cellular infiltrate in wall of bronchus, with fairly dense infiltrate in the peribronchial tissues. Exudate in lumen less cellular than in smaller bronchi.
B. 8-6 mm.	Increased thickening of wall, with hypertrophy of muscle, basement membrane, accompanied by hyaline changes. Exudate more cellular with larger numbers of lymphocytes. Lumen less dilated, more infolding of basement membrane.	Hypertrophy of bronchial muscle in evidence, with some myositis. Exudate in lumen more cellular than in larger bronchi. Epithelium flattened.
C. 6-4 mm.	Bronchi of greatest changes. Marked infolding of mucosa with collapse of bronchi. Hypertrophy and hyalinization of basement membrane. Glands hyperplastic and moderately degenerated. Marked peribronchial cellular infiltration, with large numbers of eosinophilic cells. Cartilage not degenerated. Exudate very cellular with large numbers of eosinophilic cells. No hypertrophy of epithelium. Breaking through of exudate into lumen. Hypertrophy and degeneration of muscle (myositis).	Exudate adherent to epithelium. Epithelium flattened, with areas occasionally of complete disintegration of mucosa, allowing cells to fill lumen. Exudate is layered. Muscle hypertrophy with myositis. Basement membrane degenerated, with hyaline changes. Epithelium and mucosa infolded. Total diameter increased in all this sized bronchi. Eosinophilic cells predominate both in lumen, wall, muscle, and in surrounding tissues.
D. 4-2 mm.	Moderate collapse of bronchi, moderate infolding of mucosa, hypertrophy and degeneration of basement membrane. Mucoid exudate in bronchi, with large amount of fibrin, macrophages. Occasional red blood cell in lumen. Epithelium flattened.	Changes same as in Case 1. Bronchi partially collapsed, with infolding of mucosa. Similar type of exudate as noted in Case 1. Myositis.
E. 2 mm. and less	Collapse of some, dilatation of other small bronchi. Collapsed bronchi show hypertrophy of basement membrane while noncollapsed show no hypertrophy. Collapsed bronchi show infolding of mucosa. Noncollapsed bronchi show no infolding. Moderate collapse of alveoli surrounding bronchi. Moderate cellular exudate.	Many bronchi collapsed, with infolding of mucosa, hyaline degeneration of basement membrane, and cellular exudate in lumen. Other bronchi widely dilated, no hypertrophy of basement membrane. Epithelium flattened. Mild atelectasis of surrounding alveoli.

The differentiation of the pathologic findings of the sensitive or allergic type from the non-sensitive or bacterial type of bronchial asthma by Huber and Koessler and especially by Steinberg and Figley is beset with the uncertainty as to the accuracy of the diagnosis of the bacterial asthma. In view of the occurrence of negative skin reactions to allergens, the diagnosis of non-sensitive asthma cannot be made alone on the basis of negative skin tests. Moreover Harkavy doubted the ability to differentiate the two types pathologically and thought similar changes characterize both types except for evidences and results of bronchial infection. In three of Macdonald's cases diagnosed as bacterial, marked eosinophilia was found which refuted Steinberg and Figley's deductions. Harkavy reviewed findings in 2 non-sensitive cases and concludes that the morbid anatomy was similar to that found in the obviously allergic case. These findings may indicate that bacteria can produce allergy resulting in pathologic findings similar to those resulting from food or inhalant allergy.

The debate continues in regard to the relative importance of muscular spasm and mucosal edema and secretion in the causation of bronchial asthma and secondarily of the accompanying emphysema. Walzer[2] recently reviewed the available information and favored the mechanical effect of mucus and edema of membranes. Walzer pointed out that muscular hypertrophy does not necessarily mean recurrent spasm but rather increased work arising from the obstruction of smaller bronchi resulting from membranous edema and excessive mucus. However, since bronchial asthma is undoubtedly allergic, it is reasonable to assume that smooth muscle spasm occurs in the bronchi though probably to a lesser degree than in the anaphylactic guinea pig. Walzer's statement that muscle spasm is not an important result of human allergy is debatable in view of its likely occurrence in the production of gastrointestinal and urogenital symptomatology due to allergy, and Sulzberger has recently demonstrated contractile reactions even in arterioles arising from tobacco allergy. Rackemann[10] found only moderate mucus and narrowing in the bronchi of his patient and assumed that death was due to spasm of the smaller bronchial muscles which relaxed at death. Fisher pointed to the infolding of mucosa and hypertrophy of muscle as evidencing muscle spasm as the main cause of the asthmatic breathing. Walzer, however, found evidence in the literature that some infolding of membrane occurs normally and that hypertrophy of muscle occurs in bronchitis and emphysema due to excessive work resulting from such conditions. We agree with Alexander[26] that bronchoconstriction is the result of all effects of peripheral vagal excitation which results in muscular contraction, vasodilatation and glandular secretion in varying degrees. This idea was also shared by Huber and Koessler.

Reduction in the lumina of medium-sized bronchi together with mucus in the bronchi can well account for the emphysema and asthmatic breathing. This reduction in size of the lumina can be explained by increased thickness of the lining tissues of the bronchi without the assumption of muscle spasm. But with added spasm, the constriction and potential occlusion would be increased. This narrowing and spasm of the medium-sized bronchi with possible dilatation of the small ones can also explain in part the stagnation and accumulation of bronchial mucus. In addition microscopic studies reveal the dilated mouths of mucous glands which tend to hold the mucoid excretion. These facts together with the tendency for increased viscosity and tenacity in the mucus which is not coughed up explains the formation of thick laminated adhesive mucus and of mucous plugs such as occurred in our second patient.

Effective therapy must aim at the reduction of mucus production and its elimination from the bronchi in order to increase ease of respiration and help prevent emphysema and possible asphyxia. Treatment and control of the existing allergies are of paramount importance for this result. Potassium iodide is especially helpful as an expectorant. Bronchoscopy as reported by Prickman and Vinson[24] and others helps in the actual removal of obstructing plugs of tenacious mucus and might have aided in our second patient whose bronchi were especially obstructed with tough tenacious mucus. Rackemann[18] reported death in a man of forty-seven years whose bronchial tree from the first bifurcation to the smallest bronchiole was filled with tenacious white mucus which obliterated the bronchial lumen. Case 13 of the Huber and Koessler[1] series had a similar picture, and Macdonald found mucus and fibrin filling the lumina in 3 of his 8 cases. Practically all autopsies report tough mucopurulent exudate covering or adherent to the mucosa. Where mucus is obstructing the bronchi, atropine is usually contraindicated. The colonic administration of ether and oil as suggested by Maytum[25] in severe intractable asthma is often followed by increased ability to throw off accumulated mucus. Further attempts to obtain expectorants of more value in asthma should continue. Theoretically a lysing or digesting agent acting on the bronchial mucus itself might be found which could be introduced into the bronchi by the passive method. It has occurred to us that the long continued and frequent use of adrenalin may in certain patients decrease the ability of the patient to expectorate the bronchial mucus.

Huber and Koessler after reviewing the literature and their pathological findings concluded that eosinophilia in blood and bronchial mucus was practically pathognomonic of bronchial asthma. The allergic reaction gives rise to the hematopoietic production of eosinophiles. The fact that in experimental anaphylaxis a decrease of

eosinophiles in the blood occurs with an accumulation of such cells in the shock organs probably explains the occurrence of more eosinophiles in certain tissues as compared with other tissues. However, Macdonald found eosinophiles in the spleen and thymus as well as in the bronchial tissues. Fisher and Beck found eosinophilic, plasma, and lympocytic cellular infiltration in the walls of the trachea. Murphy reported an increase of eosinophiles around the capillaries of the liver. Kountz and Alexander and Hansel especially report eosinophilic invasion present as in our second case in the mucous membranes of the nose and sinuses in patients with bronchial asthma. As already stated, Harkavy and Macdonald found eosinophilic infiltration in bronchial tissues in the non-sensitive bacterial type of asthma in contradistinction to the findings of Huber and Koessler, and Steinberg and Figley. Where eosinophilia is absent Macdonald[15] suggested the effect of a "dominant superimposed infection." Kountz and Alexander suggested that there is a special attraction between bronchial muscles and the specific allergens in asthma which results in excessive localization of eosinophiles in and around such muscles. Walzer questioned such attraction and pointed to the presence of eosinophiles in many other body tissues. More studies, however, should be made to determine if many other tissues harbor as many eosinophiles as do the nasobronchial tissues in asthmatic patients. The reason for the absence of eosinophilia in a small percentage of allergic patients is impossible to explain in light of present knowedge.

A few atelectatic macroscopic areas were observed in both our patients. Huber and Koessler reported atelectasis in two of their cases. Clarke[11] studied this result of bronchial asthma and pointed out that with partial obstruction due to constriction and bronchial mucus, emphysema results while with complete obstruction atelectasis occurs. This may be either microscopic or macroscopic according to the size of the bronchi affected.

Macdonald found the thymicolymphatic constitution as evidenced by a persistent thymus, hyperplastic lymphoid tissue and hypoplastic adrenals and aorta in each of his eight subjects. These findings were found in our second case. He suggested that allergic manifestations result from the action of allergens on an inherited constitution of this type. All other published autopsy findings are singularly free from notes in regard to this abnormality. At present Macdonald's findings need confirmation before any importance can be given them.

Neither of our cases showed definite heart lesions. In fact in our second case the patient had a small heart and aorta in spite of prolonged asthma. This coincides with the findings of Kountz and Alexander. However, other reported autopsies of patients dying of asthma showed cardiac changes. In Huber and Koessler's series there was dilatation of right ventricle in Cases 3 and 8, cardiac enlargement

and right ventricular hypertrophy in Case 10, right ventricular hypertrophy in Case 12, and dilatation and hypertrophy in Cases 14 and 15. Rackemann[10] and Harkavy in one case reported hypertrophy and dilatation of the right ventricle. Fisher and Beck's case showed hypertrophy and dilatation of the right ventricle. Macdonald found right ventricular hypertrophy in all his patients and fatty infiltration of the myocardium or patchy myocardial fibrosis in four of his eight cases and endocardial sclerosis in three of his subjects. Kountz an Alexander, however, in their excellent report of three autopsies found no evidence of dilatation or hypertrophy of the heart. Wright moreover found no hypertrophy and no pulmonary arteriosclerosis. Alexander[26] felt that reported hypertrophies were due to other causes than asthma and that bronchial asthma diminishes cardiac output thus sparing the myocardium. Harkavy suggested that superimposed pulmonary or pleural disease which diminishes the bed of the pulmonary circulation may tend to hypertension in the lesser circulation leading to arteriosclerosis in its arterial vessels. Harkavy, however, pointed out that spasmodic asthma with emphysema might produce right ventricle hypertrophy.

The contraindication of morphine in the control of bronchial asthma is emphasized by the fact that there are several reports of death attributed to the depressant effect of this drug. The asthmatic person needs to be alert and energetic so that he can use his respiratory muscles effectively and cough and raise sputum if possible. Macdonald reported one patient dying from allergic reaction to aspirin, and it is possible that Wright's patient died from the same cause. Macdonald moreover reported death in a child of thirteen years coming twenty hours after lipiodol instillation into the bronchi. The necessity of caution especially in the repeated use of lipiodol is evident. Rackemann reported 5 fatalities in women between forty and fifty years. Both of our patients were women, and 2 other patients I have seen who died in asthmatic attacks have been women between forty and fifty years.

SUMMARY

Gross and microscopic findings on two fatal cases of bronchial asthma conform with those reported by most previous observers. Evidence also points to the occurrence of myositis in the bronchial muscles. Hypertrophy and hyalinization of the basement membrane with eosinophilic infiltration were found in the antral mucous membrane. One patient had tough mucous plugs occluding most bronchi, producing marked increase in asthmatic symptoms and contributing to her death.

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DISCUSSION

DR. HARRY L. ALEXANDER, St. Louis.—I think that all these contributions are beginning to crystallize our knowledge finally on the pathology of asthma. The important thing is that people die with asthma very early, as in Huber and Koessler's case of a child where there was a just beginning hypertrophy of the bronchial muscle, and they also die after asthma of long standing associated with marked emphysema. The pathologic picture should therefore be interpreted according to the length of time patients have had asthma.

There are just getting to be enough autopsy reports to be able to find certain common factors which are very definite and which have been brought out here. In particular there are the widened basement membrane, the eosinophilic infiltration, the widened submucosal layer, the hypertrophy of muscle and degenerative mucous glands (which Dr. Rowe did not show). I think we have finally come to the point where we can say that bronchial asthma does give a definite pathologic picture as represented here.

I do not want to bring up the consideration of the cause of death from bronchial asthma because it will take too long, but I am interested in Dr. Rowe's sending out this questionnaire. When we say death from bronchial asthma, we mean that some one died in an attack of bronchial asthma or died of emphysema because he had had bronchial asthma all his life and, therefore, died from bronchial asthma. I hope Dr. Rowe will distinguish in order to get more statistics on this point, and when you answer the questionnaire, be careful to say whether patients died in bronchial asthma or as a result of bronchial asthma.

Dr. Harry L. Huber, Chicago.—It is very gratifying to me to have my work of several years ago corroborated by the essayist. I am now working on the lungs of two additional patients, both of whom had been given a narcotic by their physicians. Dr. Rowe reported the finding of areas of atelectasis. I believe these areas are very significant pathologically. They represent areas with bronchi permanently occluded by mucous plugs. Pneumonic foci often develop in these areas.

As pointed out by Dr. Kline periarteritis nodosa may be found in the lungs of practically all patients with bronchial asthma. The mucous glands in these lungs show much round cell infiltration and gland degeneration.

Dr. Joseph Harkavy, New York City.—I hope somebody who will write the final chapter on the pathology of bronchial asthma, will not base his conclusions upon one or two cases, but survey and record the various pathologic pictures of bronchial asthma, taking into account the duration of the asthma, the type, bacterial or a-bacterial, whether death was due to allergic shock, or cardiac failure, and so on. Only when one takes into consideration all these facts will one be able to talk of the pathology of bronchial asthma.

Dr. Rowe's report that the heart in bronchial asthma is small, as described by Kountz and Alexander, may be correct for certain types of cases, but it is not correct when you examine the heart of an individual who died having had asthma and emphysema continuously for twenty or twenty-five years. In such patients constant strain on the right heart is certain to bring about right-sided cardiac hypertrophy and insufficiency. The patient dies essentially of cardiac failure. Superimposed infections may frequently also play a rôle and should pneumonia supervene with death, the pathologic findings will again be different. It is obvious therefore that many factors influence the postmortem findings. I wish to point out that in studying the lungs in bronchial asthma, we should pay attention not merely to the classical description of bronchial muscle hypertrophy, changes in the alveoli and mucus secreting glands, but we should also take into consideration the effects on the vascular system of the lung as well.

In the studies which I reported, I saw definite eosinophilic infiltrations in the walls of the pulmonary arteries. It is therefore possible that allergic reactions may occur not only in the lung tissue but in the blood vessels themselves.

In view of the cumulating evidence that the vascular system may be the seat of manifestations due to hypersensitiveness, one has to take into consideration that acute death from bronchial asthma may be due not only to asphyxiation, so to speak, but also to vasomotor collapse brought about by an allergic reaction in the pulmonary vessels characterized by spasm, edema, and increase in capillary permeability. This may be followed by a fall in blood pressure, similar to that described by Coca in the anaphylactic death in rabbits and insufficiency of right side of the heart.

DR. BERNHARD STEINBERG, Toledo.—In 1929 I had the temerity to present some reports of bronchial asthma and claimed at that time that there is a definite pathologic lesion associated with this condition, and many of the members criticized the idea. I am glad to see the change in views now of the men who heard the paper and discussed it.

In 1930 I emphasized the fact that the bronchial secretion plays a distinct part in the mechanism of bronchial attack, and at that time both the western branch of the Association as well as the far eastern, attacked me quite viciously, but I think I see now the first evidences on the part of those members of the acceptance of that idea.

I received considerable criticism because of the distinction between allergic asthma and bacterial asthma. I think I deserved some of it. The case of asthma which we studied was so remarkable, the condition which we labeled as bacterial asthma was so unlike any other condition of lung which we have seen, we were compelled to believe that this particular instance was of so-called bacterial asthma. In retrospect one could say that the case of bacterial asthma was a hyperplastic process in which the bronchi were completely occluded by connective tissue. In the true allergic type, the bronchi are partly or completely occluded by mucus, but the end-result is the same. The pictures, as far as the clinical story was concerned, were alike, and we concluded we were apparently dealing with some form of asthma.

I think it remains for the future and further investigation of similar cases, especially of postmortem material, to determine whether there is actually a pathologic basis for the so-called bacterial asthma.

DR. ROBERT WARD LAMSON, Los Angeles.—I recently reviewed 116 histories of patients classified as "fatal asthma." That is, asthma was considered the primary or the contributory cause of death. The majority of these were county hospital patients, and the deaths occurred during the past six years. Dr. Alexander just emphasized a very significant point, namely, that one should distinguish between those that died "from" or because of bronchial asthma, and those that died "with" it. My series, as well as the reports previously published, contain both types of patients. The cases might be subdivided into two groups: (1) not autopsied—83 patients, and (2) autopsied—33 patients.

As Dr. Rowe has stated, the literature contains reports of 40 or more patients with asthma who came to autopsy. Several writers have summarized these, but they differ as to what cases should be included

under the heading of bronchial asthma. For example, Dr. Rackemann's case was not included in those described in Coca's book, while others have excluded some of those listed by Coca. Steinberg states that most authorities finally exclude all but 16 of the published reports. If we are to study the pathologic condition of asthma, we should, if possible, differentiate between the several clinical types of this condition. In reviewing the literature, I found reports of 41 patients, including Dr. Rackemann's, which justified a tentative diagnosis of bronchial asthma. These were considered more or less standard and, with my own series, were subjected to statistical analysis.

A separate chart was made for each of the following: males not autopsied, males autopsied, males (autopsied) already reported. A similar series of female patients was prepared. Bar diagrams were employed to show the age at death and the duration of symptoms, if given. The data were arranged in ascending order of age at death. Another feature considered was the duration of symptoms in each of the six groups. (Lantern slides of these charts were demonstrated, but they need not be reproduced here, as they will be included in the final report.) A brief summary of these data may be pertinent. Many of the patients lived well beyond the age of fifty years—several of them in spite of "asthma" for the greater portion of their life. This clinical syndrome is not without its hazards, however, as will be indicated in Table I.

TABLE I

DURATION OF ASTHMA

DURATION	MALES			FEMALES		
	NOT AUTOPSIED	AUTOPSIED	PREVIOUS REPORTS	NOT AUTOPSIED	AUTOPSIED	PREVIOUS REPORTS
5 years or less	42%	47%	61%	40%	38%	43%

If those previously reported are true bronchial asthma, then the condition may be fatal in most patients within five years of its onset. The agreement between these figures and those in my series (both groups) suggests that my cases are similar. If there is a characteristic pathologic lesion, how long does it require to develop it, and is it the cause or the result of the symptoms, and may it explain the fatal termination? A duration of five years does not imply constant symptoms during that period. In this study I am fortunate in having the cooperation of Dr. I. G. Macdonald, who, as Dr. Rowe has stated, is responsible for eight of the previously reported cases. We have not yet reached an agreement on the question of cause and effect. His concept of the fundamental pathology is essentially that just demonstrated by Dr. Rowe. In addition, he supports the theory that all patients having this pathology have also a persistent thymus and a generalized hyperplasia of the lymphoid tissue. From a clinical standpoint, Old and also Dublin conclude, from their study of life insurance statistics, that "heart disease mortality" in asthmatic persons is from 2 to 3¼ times normal. If they are studying true asthmatic individuals, then one would expect a preponderance of cardiovascular pathology at autopsy. These divergent views make it especially important that future autopsies be complete, and not alone a study of the lungs.

Mucous plugs in the bronchi were mentioned by a previous speaker. A recent case of ours, a composite textbook picture of all Dr. Macdonald has emphasized, demonstrated this to a marked degree. The plugs had become canalized, much as a thrombus may in the vascular tree, and suggest that they had been present many years. These canals were, in turn, filled with very tenacious mucus, probably of recent origin. Mechanical obstruction was an important factor in the fatal termination.

DR. BRET RATNER, New York City.—Ever since Meltzer expressed the belief that the symptoms in the anaphylactic guinea pig were identical with bronchial asthma, and the whole mechanism of allergy depends so largely on the fixation of antibodies to smooth muscles in the bronchioles, it has seemed to me that the pathology of asthma should be viewed as one of disturbed function rather than an organic change.

It seems to me that the work presented this morning is a little misleading and should be really relegated to the complications of prolonged asthma. I, for one, should like to see a case presented of a child who actually died after the first or second attack of acute asthma.

In attempting to study the pathology in experimental asthma in the guinea pig, we took animals that died after inhalation, fixed the lungs, did pathologic specimens, and found absolutely nothing. The spasm was relieved, and the lungs, to all intents and purposes, were perfectly normal except for the breaking of alveoli; so it seems to me as we progress in allergy we ought to adhere to fundamental differential diagnosis and not talk about conditions that are complications or sequelae of asthma, rather than asthma itself.

DR. WARREN T. VAUGHAN, Richmond.—I call your attention to the article by J. Alexander Clarke, about a year ago, in which he emphasized that this appears to be an entirely different type of asthma, an asthma which is entirely intractable, of relatively short duration, and often results in death.

In the last fourteen years we have seen four deaths in acute attacks of asthma. All of them were asthmatic individuals of relatively short duration, less than four years. These four cases have some interesting points, and I am going to mention them briefly because they illustrate some factors in the causation of death that have not been brought out this morning. We had an autopsy on only one case, of two years' duration. At autopsy there was nothing. There were no mucous plugs, no secretion, no bronchitis, the bronchial tree was dry. There were low grade microscopic changes. It is interesting that the patient had previously had many attacks of asthma as severe as her final, fatal attacks.

During the last attack I was out of the city and she was taken to a hospital. The physician, feeling that she had had asthma for so long that her heart must be getting weak, thoroughly digitalized her. Hers was the smallest heart for a person of her size that I have ever seen. She died, in my opinion, of digitalis poisoning.

The second case brings out another point. A young lady with extensive sinus infection, who had been treated by a nose and throat specialist for a long time, without any improvement whatsoever, was found sensitive to dust. Under treatment she was doing beautifully.

She went in to pay her bill to the nose and throat doctor who said, "Let me look in your sinuses." She had no symptoms. He said, "You still have a lot of trouble," and he did some more probing. Within a few hours she had a severe attack of asthma, and within twelve hours she was dead. This emphasizes the desirability of not meddling if the patient is doing all right.

The third case was that of a woman who had cardiac valvular disease. The acute asthmatic attack was too much for her heart. She died a cardiac death.

The fourth was unexplained, though we had reason to suspect it was after an overdose of morphine, self-administered.

DR. GEORGE L. WALDBOTT, Detroit.—I should like to bring up a point which I think is very important. If you look over the literature on asthma—and this was also brought out by Dr. Lamson's table—you will find that there are very few children, only 2 in about 50 cases reported in Walzer's book, who died from asthma. I think this is very significant. It indicates that either children do not die from asthma, or that asthmatic death is not recognized in its early state because its pathologic condition is different in children than in adults. I shall shortly publish more definite proof to substantiate the following fact:

In a patient who has had asthma for a long time, certain changes have developed in the lungs which indicate a tendency of adjustment of the system, particularly of the lungs to continued exposure to antigen, such as to contact with inhalants, to infections, etc. A child has not had a chance to undergo such changes, and that is the reason why a child dies suddenly, presenting the earmarks, not of asthmatic death, but of so-called thymic death, or anaphylactic shock. Edema in the lungs is the main finding, and this resembles closely the changes found in anaphylaxis in dogs. In other words, death from asthma in its earliest state resembles anaphylaxis.

I feel that this observation constitutes a missing link in our conception of allergy. It explains that the apparent difference between anaphylaxis and allergy depends primarily on whether or not there is a more or less continuous exposure to antigen. By the readjustment of the system to this exposure the effect in the human being is a different one than that in an animal which has been made sensitive two to three weeks previously and is then shocked by a comparatively tremendous overdose.

DR. ROWE.—Our manuscript contains a discussion of the cardiac pathology found in bronchial asthma, and is largely in accord with the conclusions previously published by Alexander and Kountz. Our findings in part corroborate those found in the thymus and aorta as reported by Dr. McDonald in his contribution on the subject.

PHYSICAL ALLERGY*

Its Rôle as Manifested in the Routine Study of 325 Consecutive Allergic Cases

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IT CANNOT be denied that abnormal responses to normal environmental heat, cold, and sunlight occur. These abnormal responses by definition constitute physical allergy. Duke,[1] in a series of brilliant clinical studies, has described in detail the symptoms, signs, electrocardiographic changes, diagnostic criteria and tests, therapeutic principles, and his theory of the pathologic physiology of the various manifestations of physical allergy. The clinical aspects of his theses have been confirmed, in the main, by Bray,[2] Alexander,[3] Weiss,[4] Wilson,[5] Hopkins and Kesten,[6] Morey and Michie,[7] Horton and Brown,[8] Swineford and Weinberg,[9] Harris, Lewis, and Vaughan,[10] Hill and Clement,[11] Mollison,[12] and numerous others who have reported manifestations of physical allergy in the skin, nose, bronchi, and systemically. Covisa and Prieto[13] claimed to have accomplished passive transference of hypersensitiveness of the skin to cold. Spiesman[14] showed that the nasal mucosa in vasomotor rhinitis responded erratically to moderate thermal stimuli, whereas the infected mucosa did not respond at all. Peters and Hoffman[15] in a preliminary report of several cases of physical allergy showed that, during attacks of hay fever and asthma, heat produced a decrease in body temperature and ice rubs caused a rise in temperature. When the same patients were feeling well and were free from symptoms, the heat would raise the temperature and the ice would lower it. It is not improbable that experimental evaluation of Duke's hypothesis† that the manifestations of physical allergy are due to a disturbance of the heat regulating mechanism will develop from the studies by Lewis[16] and his coworkers of the effects of the histamine-like substance liberated by the skin in response to injury.

Duke has not, nor has any one, attempted to evaluate the rôle of physical allergy in any consecutive series of allergic cases. It would seem desirable, then, to begin statistical comparisons between physical and material agents, such as foods, inhalants, drugs, contact substances, and bacterial products, as exciting factors in large groups of allergic manifestations. In this report there is a detailed analysis of the rôle of

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†The exposition and diagrammatic summary of Duke's theory of the pathologic physiology of physical allergy which was presented as a part of the original paper, is omitted with the author's permission.

physical influences so far as it can be determined by history alone in 325 consecutive cases and by routine physical tests in 63 cases.

The routine allergic history employed in the Allergy Clinic of the University of Virginia Hospital includes a discussion of the effects of various physical influences as well as a detailed analysis of the effects of foods, inhalants, focal infections, drugs, contact substances, environmental hazards, etc. In taking a physical allergy history the patient is asked whether any untoward symptoms result from or are aggravated by draughts, getting his feet wet, undue fatigue, exercise, emotional strain, relaxation, temperature changes (sudden, daily, or seasonal), hot or cold baths, dampness, sunlight, pressure, or friction.

The rôle of physical factors in 325 consecutive allergic patients as determined by history alone is analyzed in Table I. When grouped by

TABLE I

ANALYSIS OF RÔLE OF PHYSICAL FACTORS IN 325 CASES AS DETERMINED BY HISTORY ALONE

CHIEF COMPLAINT	ASTHMA	HAY FEVER	URTICARIA AND ANGIONEUROTIC EDEMA	ECZEMA	MIGRAINE	MUCOUS COLITIS	TOTAL
No. Cases	110	135	30	18	26	6	325
RÔLE OF PHYSICAL FACTORS							
On Chief Complaint							
Initiate	44	26	6	2	16	1	95
Aggravate	37	51	6	8	2	2	106
Importance: Chief	0	1	0	0	2	0	3
Importance: Major	41	29	8	6	13	2	99
Importance: Minor	40	47	4	4	3	1	99
Importance: Negligible	29	58	18	8	8	3	124
On Other Allergic Symptoms	22	10	2	0	3	1	38
OTHER IMPORTANT FACTORS							
Foods	48	20	22	8	12	6	116
Inhalants	88	98	1	0	2	2	191
Foci	17	7	7	2	6	1	40
Contacts	0	1	1	5	0	0	7

chief complaints 110 were asthma, 135 hay fever, 30 urticaria and angioneurotic edema, 18 eczema, 26 migraine, and 6 mucous colitis. Physical factors seemed to initiate the chief complaint in 95 and to aggravate it in 106 cases, a definite rôle in 201 of 325 cases. In only 3 cases were physical factors thought to be of chief importance. In 99 they were considered of major and in 99 others of minor importance. The effects of physical factors seemed negligible in 124. In 38 cases symptoms other than the chief complaint were attributed to physical agencies. In other words, 22 patients with asthma, 10 with hay fever, 2 with urticaria, 3 with migraine and 1 with mucous colitis had other symptoms from physical causes. The attempt was made to evaluate, by history alone, the rôle of other etiologic factors, such as foods, in-

TABLE II

ANALYSIS OF SYMPTOMS ATTRIBUTED TO PHYSICAL FACTORS BY 325 PATIENTS

SYMPTOMS PHYSICAL INFLUENCE	SNEEZE	NASAL CONG.	"FRESH COLD"	COUGH	WHEEZE	HEADACHE	VERTIGO	HIVES	ANGIO	ECZEMA	"SHOCK"	ABD. CRAMPS	NAUSEA AND VOMITING	JOINT SYMPTOMS	TOTAL
Draughts	9	32	17	9	16	6	0	0	0	0	0	0	0	0	89
Wet feet	4	5	12	5	13	1	0	0	0	0	0	0	0	0	40
Sunlight	9	2	1	0	0	2	0	2	1	1	0	0	0	0	18
Exercise	4	14	5	8	29‡	5	0	1	0	1	0	0	2	0	69
Excitement*	4	6	0	2	21	13	0	1	1	1	0	0	0	0	49
Fatigue*	1	6	3	1	23	16	0	1	0	0	0	0	1	1	53
Inactivity*	0	3	0	0	1	0	0	0	0	0	0	0	0	0	4
External dry cold	2	10	2	2	18	0	0	2	0	0	0	0	0	0	36
External dry heat	2	10	0	2	19	7	0	3	0	3	0	0	1	0	47
Cold baths	2	1	1	2	5	0	0	2	0	0	3	1	0	1	18
Hot baths	0	2	1	0	1	0	0	4	1	1	0	0	0	1	11
Hot to cold†	6	23	6	7	18	0	1	0	0	1	0	0	0	0	62
Cold to hot†	1	12	4	2	8	0	0	1	0	2	0	0	1	1	32
Humidity	3	9	1	4	14	1	0	0	0	0	0	0	0	0	32
Cold and damp	2	14	8	4	32	1	0	0	0	0	0	0	0	0	61
Pressure, blows or friction	3	1	0	0	1	0	0	3	0	0	0	0	0	0	8
Total	52	150	61	48	219	52	1	20	3	10	3	1	5	4	629

* Although these are not truly physical agents, they are included in conformity with Duke's outline.
†Day, air, or water.
‡Two of these only when in cold air.

halants, focal infections, and contact substances. It will be seen that foods were thought to be significant in the causation of the chief complaint 116 times, inhalants 191 times, focal infections 40 times, and contact substances 7 times. These figures should be contrasted with the 201 cases in which physical factors seemed important. Migraine is of particular interest in that physical factors were thought to be of chief or major importance in 15 of 26 cases.

The incidence of different symptoms attributed by the 325 patients to various physical factors is given in detail in Table II. The symptoms and physical influences are self-explanatory. Duke[1] has reported an even greater variety of symptoms from physical tests in his laboratory. The important and significant result of this analysis is that 325 patients attributed 14 symptoms to 16 normal environmental physical influences a total of 629 times.

For about eighteen months most of our patients with histories suggestive of physical allergy have been tested with heat, cold, and ultraviolet rays. The tests consisted of ten-minute exposures to infra-red heat and ten-minute contacts with iced wet towels, each being applied to the chest and to the other areas suggested by the history. When positive, the test was ended, immediately upon the appearance of symptoms, by applying the opposite thermal extreme. Ultraviolet was used only when the history indicated hypersensitiveness to sunlight. Occasionally patients were tested with mixed thermal extremes, i.e., cold air to the nose and mouth, while the chest was exposed to heat, and vice versa. The tests were purposely kept within this simple routine. No effort was made to determine the effects of draughts, wet feet, humidity changes, exercise, or baths, which the histories suggested as potential initiating or aggravating factors of the chief complaints.

An analysis of the rôle of physical factors in 63 allergic cases as determined by routine physical tests alone is summarized in Table III. The tests were for asthma as the chief complaint 29 times, hay fever 17 times, urticaria and angioneurotic edema 8 times, eczema 1 time, migraine 5 times, and mucous colitis 3 times. The chief complaint was reproduced markedly in 11 (18 per cent), moderately in 30 (48 per cent), and negligibly or not at all in 22 (35 per cent) of the cases. It is of interest that symptoms other than the chief complaint were caused 11 times (18 per cent). In the 11 cases which reacted markedly the symptoms were distressing to the patient. In the 30 moderate reactions the patient either had distinct nasal blockage, became hoarse, coughed, wheezed, had a skin eruption, or complained of headache or abdominal pain. In those negligibly affected there was either no reaction or one which was not definite enough to be considered more than coincidental.

The effective test was ice in 30 cases, infra-red in 14 and ultraviolet in 3. When symptoms appeared, the effective influence was immediately replaced by the opposite thermal extreme, and relief or failure to

relieve was noted. Relief was thus obtained promptly in 36 of 44 reactions to ice or infra-red. The history and tests agreed 34 times. The important and significant result of this analysis is that in 63 simple

TABLE III

ANALYSIS OF RÔLE OF PHYSICAL FACTORS IN 63 CASES AS DETERMINED BY ROUTINE PHYSICAL TESTS ALONE

CHIEF COMPLAINT	ASTHMA	HAY FEVER	URTICARIA AND ANGIONEUROTIC EDEMA	ECZEMA	MIGRAINE	MUCOUS COLITIS	TOTAL
Total No. Tests	29	17	8	1	5	3	63
Results of Tests							
Reproduced Chief Complaint							
Markedly	4	3	2	1	1	0	11
Moderately	14	9	3	0	2	2	30
Negligibly	11	5	3	0	2	1	22
Reproduced Other Symptoms	2*	5*	1	0	2*	1	11
Effective Test							
Ice	15	9	1	0	3	2	30
Infra-red	5	6	3	0	0	0	14
Ultraviolet	0	0	2	1	0	0	3
Relief by Opposite Factor	18	13	2	0	2	1	36
History vs. Test							
Agree	18	11	2	1	1	0	33
Disagree	11	6	6	0	3	4	30

*Other symptoms were produced concomitantly with asthma once, migraine and hay fever twice each.

tests the chief complaint was appreciably reproduced 41 times and other symptoms 11 times.

The individual symptoms reproduced by the simple physical tests are presented in detail in Table IV. It will be seen that nasal con-

TABLE IV

ANALYSIS OF SYMPTOMS PRODUCED BY 63 ROUTINE PHYSICAL TESTS

SYMPTOM	NASAL CONGESTION	COUGH	WHEEZING	HEADACHE	URTICARIA	ANGIONEUROTIC EDEMA	ECZEMA	ABDOMINAL CRAMPS	HOARSENESS	TOTAL
Test										
Infra-red	13	1	4	1	0	0	0	0	0	19
Ice	5	8	10	6	2	0	0	4	1	36
Ice and Infra-red simultaneously	2	1	0	0	1	0	0	0	0	4
Ultraviolet	0	0	0	0	1	1	1	0	0	3
Total	20	10	14	7	4	1	1	4	1	62

gestion occurred 20 times, cough 10, wheezing 14, headache 7, urticaria 4, abdominal cramps 4, and angioneurotic edema, eczema, and hoarseness once each, a total of 62 symptoms in 63 tests. The effective test was infra-red in 19, ice in 36, both simultaneously in 4, ultraviolet in 3.

The apparent discrepancy in the totals, when compared with Table III, is due to the fact that in several tests more than one symptom was noted.

DISCUSSION AND SUMMARY

The importance of physical agents in the production of so-called allergic manifestations can be determined by comparing physical and material histories, by reproducing and relieving the symptoms by physical tests, and by comparing therapeutic results from physical therapy with those based on skin tests, elimination procedures, etc. Several factors will prevent numerical accuracy in such a series of comparisons. For example, any history may be inconsistent with subsequently proved facts; symptoms reproduced by physical means might also be reproduced in the same patient by material means; or specific treatment by material means might raise the threshold of response to physical agents and vice versa.

The data upon which this report is based do not include any therapeutic comparisons and are presented with full appreciation of the pitfalls attendant upon an attempt to evaluate the histories and tests. However, in spite of possible inaccuracies in individual instances, it cannot fail to be significant that in the routine study of 325 consecutive allergic cases: (1) 201 patients attributed an appreciable amount of their trouble to physical agents, more often than to any one group of material agents; (2) 325 patients attributed 14 symptoms to 16 normal environmental influences 629 times; (3) the chief complaint was reproduced appreciably 41 times and other symptoms 11 times in 63 simple physical tests; (4) 9 symptoms were produced a total of 62 times in 63 tests; (5) 36 of these 62 symptoms were relieved promptly by the application of the physical (thermal) influence opposite to that which produced them.

The purpose of this paper will be accomplished if it stimulates the widespread inclusion of physical histories and tests in the routine study of allergic cases. If it does, sufficient data should soon be available for a more accurate evaluation of the rôle of physical allergy in the allergic diseases and for the evolution of a theory which will explain, logically, the facts of both physical and material allergy.

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DISCUSSION

DR. HARRY L. ALEXANDER, ST. LOUIS.—I think these are very interesting observations, and there is no question about the results that have been found. I may, however, take exception to the title of this paper, namely, "Physical Allergy," and I wonder whether it would not be a little safer to say "Physical Factors in Allergy."

That there is such a thing as physical allergy is undoubted. The urticarias that we see, particularly coming on with heat and cold, are physical allergy. Now, with some of the symptoms here reported, one may ask the question whether, if a patient was allergic to horse dander and he wheezed in the cold air, he was a case of physical allergy. I noticed that migraine was cited 13 times as due to excitement. Is that physical allergy?

I think the observations are interesting, but we should be careful in interpreting them because we should like to separate physical allergy from the other type of allergy due to known allergens.

DR. GEORGE PINESS, Los Angeles.—I should like to ask Dr. Swineford whether those patients who reacted to allergens as well as to physical factors were relieved by elimination of or treatment with the allergens to which they reacted. All of us have seen and observed such patients who give this history of heat and cold sensitivity who are benefited by specific treatment whether it be elimination or desensitization with the specific substances, without considering the physical element involved.

Dr. Duke is deserving of a great deal of credit for bringing to our attention this interesting and complex problem of physical allergy which we know so little about. Dr. Swineford has attacked this problem most intelligently, and it should bring forth results and information that will lead to a better understanding of this very interesting phenomenon.

Dr. Harry L. Huber, Chicago.—Last year I read a paper entitled "Nonallergic Vasomotor Rhinitis," and in it pointed out the characteristic findings in this group of patients. Many of the patients that Dr. Swineford describes fall in this group. They are sensitive to temperature changes, have a low blood pressure, and in general are below par. There are no significant positive skin reactions. There is a very low familial incidence of allergy. In many respects these patients differ from the true allergic patients. They are sensitive to cold, to heat, or to other physical factors. The relationship of the endocrine gland to the heat regulating mechanism was mentioned, and I believe this relationship is of great importance in this group of patients.

I should like to ask Dr. Swineford whether he has made a special study of the group that does not exhibit positive skin reactions, and whether he has found a difference in his examination of this group as compared with those where there are typical positive skin reactions. This difference is very important clinically.

Dr. Milton B. Cohen, Cleveland.—That these physical factors play a part in the production of symptoms in patients who have other types of allergy there can be no doubt. Dr. Rudolph and I were much interested in this a number of years ago, shortly after Dr. Duke began the work, and we planned some experiments in which we took patients who were sensitive to certain things, inhalants particularly, and who then gave either histories or actual symptoms on exposure to physical agents, and put them in an environment where it was impossible to breathe in the inhalant factors. We found in the several we so studied that when you take the patient away from the inhalant to which he is sensitive, and which is primarily responsible for his symptoms, you cannot give him the symptoms which, when you exposed him to the same physical agents, had previously given him symptoms.

In addition to the work reported by Dr. Kline, we excised some wheals produced by heat and cold in individuals who apparently had only heat and cold hives, and were much astonished to find that the histologic reaction underlying those wheals was quite different in extent from that which occurs in the individual who has hives or a reaction on top of a sensitivity of another type. These tissues which we removed showed responses quite like those histamine would produce in a normal individual, and not like those histamine would produce in an individual who was sensitized.

Dr. Swineford.—I agree to the alteration in the title, and I hope that Dr. Alexander will change it when it comes to publication. I do not know that it is entirely necessary, though, because the term "physical allergy" in its literal sense means, simply, an altered reaction to physical agents. These patients all seem to have an altered reaction to physical agents and are, therefore, the victims of physical allergy.

Dr. Piness asked whether we had observed alterations in the threshold of response to physical influences after removing offending foods and

inhalants. I believe Dr. Cohen and Dr. Huber also raised this question. We have not studied this. It is quite a common and somewhat analogous observation, that patients who have pollen hay fever will also have symptoms during the pollen season from feathers or foods or what-not, which they will not react to clinically at other times of the year. This is one of the most widely accepted reasons for failure to get good results from the pollen treatment during the pollen season. Now, it is conceivable to me, though I cannot say that it is a fact, that specific material treatment will raise the threshold of response to physical factors and, conversely, that treatment with physical factors will raise the threshold of response to material factors. This remains to be seen.

Dr. Huber asked whether we had made a special study of the skin-negative patients. We have not. That is one of the things we plan to do, and we hope in the not too distant future to have 10 or 15 cases from this series worked out completely with comparisons of skin tests and therapeutic results. We have quite a few patients who have rather interesting therapeutic results which we are not ready to report now.

TECHNIC ON INTRACUTANEOUS TESTS AND RESULTS OF ROUTINE TESTS IN NORMAL PERSONS*

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FOR some time we have observed that many patients seem to have an "irritable skin"; they show positive reactions to a variety of substances when tested intracutaneously with the extracts. We have tried to explain this irritable skin in various ways but without much success. Occasionally the patient would show a marked redness and swelling after simple stroking of the skin, but true dermographia of this sort was the exception and not the rule.

In the meantime, we had been making our tests with syringes which had a metal plunger wound with asbestos thread, chiefly because such syringes cost about one-fourth of the price of all-glass syringes and because they were easier to handle. We began to suspect our syringes; that their use resulted in a chemical contamination of one allergen with another. Tests with serial dilutions of ragweed have shown that certain patients are so sensitive that they will react to a dilution as high as one to a million. In such a case, it is easy to see that a very little contamination of another allergen with ragweed would easily give a positive test which would be false. Incidentally, boiling reduces the skin test activity of our ragweed solution very little, if any. Our asbestos syringes were tested with methylene blue, and it was found quite impossible to wash the syringe free of color with anything short of heroic measures. When later we found that a set of new syringes gave quite different and reasonable results, the need of change to a new technic became imperative.

During this past year, all our intracutaneous tests have been made with all glass syringes. More than that, no syringe is now used for more than one allergen. This segregation is made easily possible by the use of a special rack made of wood (Fig. 1).

The baseboard, 16 inches long by 10 inches deep, carries two stringers 2½ inches apart between centers. Each stringer is an inch high and has twenty notches each ¾ inch apart between centers. (The stringers are made by boring ½ inch holes with centers ¾ inch apart down the middle of a two-inch strip and then sawing the strip in two.) In the back of the base, holes for bottles are bored on centers 1½ inches apart—in two staggered rows, the holes being placed so

*From the Anaphylaxis Clinic of the Massachusetts General Hospital.
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that each syringe points straight to its corresponding bottle and therefore is labelled automatically.

This rack is very useful in the Clinic and can be easily carried to the wards. The syringes are filled each morning and suffice for at least 12 and often 16 or more patients. Newly boiled needles are applied frequently though we often test two patients at once with the same needle.

Since this technic has been employed, the number of "irritable skins" has been markedly reduced. When they are found, simple scratching of the skin will also cause reactions because the patient has dermographia. The positive reactions which we do obtain seem to "make sense" in a majority of the cases.

Meantime, our new technic has been used to test normal nonallergic patients as found on the medical and surgical wards. Sixty patients have been tested with a selected group of nine allergens, arranged in

Fig. 1.

this order: ragweed 1:1,000; horse serum 1:100; normal saline; wheat extract containing 0.02 mg. N per c.c.; silk floss 0.02 mg.; cat hair 0.02 mg.; feathers 0.02 mg.; timothy 1:1,000; and orris powder 0.02 mg. The results are interesting and surprising in that a goodly number of the supposedly nonallergic individuals gave positive reactions. Indeed, out of the whole list of 60 persons, only 30 (one-half) gave entirely negative results.

Ragweed produced a definite immediate wheal and erythema response in twelve patients (20 per cent); only two of these had a family history of allergy; another was a woman with pernicious anemia who after the test declared that she had hay fever in August. Two others had had hay fever in times past. The rest, however, were unaware of their sensitiveness. Horse serum reacted in four patients (6.6 per cent), and in an additional series of 22 patients the same 1:100 dilution of horse serum injected intracutaneously produced slightly positive reactions in three (15 per cent). Normal saline was

negative in all 60 persons. Wheat reacted three times (5 per cent); one a man with peptic ulcer and no history of allergy; in the woman with hay fever noted above; and in a girl with arthritis. Silk floss—a crude extract made from the contents of an old kapok pillow—was the chief offender. It showed definite reactions in 22 persons (27.3 per cent). Cat hair extract produced a wheal in four patients (6.6 per cent), at least one of whom admitted sensitivity to cats. Feathers reacted only once (1.6 per cent). Timothy reacted seven times, and at least three of the seven patients agreed that they had or had had symptoms of early grass hay fever. Orris powder extract was next to silk floss and ragweed in the frequency with which it produced positive reactions. Ten of the 60 individuals (16 per cent), six women and four men, gave definite wheal and erythema reactions to orris powder, but except for one who had hay fever none of them admitted having any allergic disease.

A general irritability of the skin was observed in four patients who gave larger or smaller reactions to every substance injected except normal saline. One was the anemia patient with hay fever mentioned above; another was a woman of twenty-five years with osteomyelitis; a third was a man with heart disease and a history of former hay fever; the fourth was a girl with gastric symptoms but no allergy.

DISCUSSION

These results are surprising, as said. The number of cases is not large enough to justify any close analysis of the precise findings, but it is large enough to indicate certain broad principles in the study of allergy. They show that clinical allergy is even more common than expected. Here is a group of 60 persons entering the hospital with various diseases not at all concerned with allergy and yet skin tests made in a purely routine manner with a few simple substances bring out the fact that at least four of the sixty (6.6 per cent) have hay fever and that one of them is clinically sensitive to cats as well as to pollen. The results make it still more difficult to make a clinical distinction between those persons who are allergic and those others who are supposedly nonallergic or normal. In the Prausnitz-Küstner reaction, we transfer the sensitiveness to the skin of a "normal recipient." Evidently, it is not easy to be sure that the "normal" is normal. Controls become of greater importance.

The large number of positive reactions following the injection of certain allergens like silk floss, ragweed, and orris powder is difficult to explain. Perhaps the extracts were irritating, but even the silk floss reacted in only a little over one-fourth of the cases. Obviously, it was not irritating to all.

Finally, it is evident that most of the reactions observed had no clinical significance whatever. This confirms our impression in clini-

cal allergy that many positive tests are obtained but few of them are valuable. How shall the others be explained? The question cannot be answered now.

SUMMARY

1. In making intracutaneous tests, the importance of chemical as well as bacteriologic cleanliness is emphasized. The need for all-glass syringes is defined, and a convenient rack for segregating and labelling the syringes is described.

2. When this improved technic is applied to the study of normal, nonallergic individuals, many positive skin tests are obtained.

3. The importance of this observation to the study of allergic patients is discussed.

DISCUSSION

DR. SAMUEL FEINBERG, Chicago.—I do not think it is fair to the patient to give him any kind of injection without boiling the syringe which has been used on previous patients. While it may take more time to wash out that syringe and boil it, I think it is worth the effort.

You must realize that patients may become infected, although it may be rare. I do not mean ordinary suppurative infections but I mean other infections, such as malaria, for example. We have had the experience at the County Hospital in Chicago that patients have come in with malaria which can be traced to hypodermic needles. These patients are addicts who are accustomed to gather in parties and to inject themselves intravenously with heroin or morphine, using the same syringe and needle.

But it is conceivable also that if the needle were changed, they would get enough seepage into the syringe that one does not know about and cannot see which may be sufficient to infect the next patient, and I do not believe it is fair to treat patients without changing the syringe. It takes much more time to have a large number of syringes and keep them washed out and reboiled before treating the next patient, but it is worth the effort.

DR. ROBERT WARD LAMSON, Los Angeles, Calif.—I believe it is not an uncommon practice, when doing a large number of Schick tests, to use, without repeated sterilization, the same syringe and needle, wiping the latter with an alcohol sponge after each test. If this method has proved satisfactory in pollen and Schick tests, possibly we should not condemn it too vigorously.

Dr. Rackemann indicated that he does not measure the quantity injected but judges the amount to use by the size of the welt. Many of us follow the same technic. This leads me to offer a suggestion which may reduce the cost factor in the use of all-glass syringes. Ungraduated 1 c.c. tuberculin syringes can now be obtained. The initial cost is less than that of the graduated syringes, and the unbroken part of a syringe, either barrel or plunger, may be saved and turned in for some credit. If these were graduated syringes, only the plunger has this refund value.

DR. ARTHUR F. COCA, New York.—I thought Dr. Piness might allow me to state in my own defense that I have used all glass syringes since two or three years before I left New York Hospital. At about that time Dr. Donnally was telling me about the trouble he had in his work with the highly egg-sensitive children, and his study of the elimination of egg protein in mother's milk. He had to take a special precaution in cleaning his glassware to prevent these contamination reactions. So, as far as I am personally concerned, I perfectly agree with Dr. Rackemann that the asbestos plunger is disadvantageous for practice.

Besides that, I do not know whether Dr. Rackemann made the point that boiling of these extracts does not very much alter their specific reactivity, in many instances. Dr. Wodehouse was the first to point that out with respect to the vegetable extracts, and I have seen that heating pollen extracts in neutral solution at 100° C. for a half hour does not very greatly diminish the specific reactivity.

I want to ask Dr. Rackemann whether he was able to transfer passively the reactions that he had in the normal series.

DR. BRET RATNER, New York City.—Dr. Coca brought up the point about the difficulty of getting rid of the proteins in syringes. In working with milk we found that ordinary boiling did not affect the antigenic character of casein. You can boil it for hours, and it still remains highly anaphylactogenic, so we made a practice of having all glassware, after being thoroughly cleaned, put in the cleaning solution for twenty-four or forty-eight hours before using it again.

DR. MARION B. SULZBERGER, New York City.—I should like to agree with those who contend, as Dr. Rackemann does, that the factor of contamination of the syringe may be important in the variations of results in skin testing. Fortunately, I believe the testing of atopic conditions does not generally require one to meet such high degree of hypersensitivity as is the case, for instance, with tuberculin. That may sound like a bold statement, but compared to tuberculin hypersensitivity the degree of skin hypersensitivity in atopic conditions is generally less. Those who have been doing quantitative tuberculin tests for years have made it a rule to be even more rigid than Dr. Rackemann in trying to prevent syringe contamination. With tuberculin it is a necessary rule not to use a syringe that has been used for a higher concentration in testing with a higher dilution: one that has been used for a 1:100 cannot be used for 1:1,000,000 dilution, because it has been found that the factor of error continued in that syringe *even after repeated boiling and washing.*

DR. RACKEMANN.—I simply wanted to bring the subject up because I happen to know that a good many men are still using syringes wound with asbestos for doing their tests. In our clinic the results are better and easier to interpret since we have been much more careful about the technic of making the test.

I thank Dr. Coca for reminding me of boiling. Boiling does not affect ragweed or some other substances. As for contaminations, as far as we know, everything goes out of the needle and we do not think anything comes back further than through the needle itself, and then we have a new needle. The proof of the pudding is always in the eating and the fact is that we have no trouble from contamination.

STATUS ASTHMATICUS*

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RELATIVELY speaking, status asthmaticus is not encountered frequently, but it presents an alarming picture when it does occur. Drugs normally relieving asthmatic attacks are of no benefit in status asthmaticus, nor do they show any definite pharmacologic action.

The modus operandi of status asthmaticus is not known, but (1) an excessive and massive dose of an allergen (atopic reagin), (2) an essential allergy of previously injured tissue, and (3) changes in the functioning of neurotropic or humoral mechanisms may all play a part.

The report of Case 1 may demonstrate that an excess of allergen can serve as a responsible factor in status asthmaticus.

CASE REPORTS

CASE 1.—Eight years ago (1926) a man twenty-eight years old, who had recently arrived from England, came to the dispensary for treatment. He had suffered from asthma over a long period of years. At that time he was working in a cigar store located in a fur district in Philadelphia. He was sensitive to rabbit hair in dilution of 1:100,000. He was free from asthmatic attacks when away from the district or when out of town, and attacks usually occurred while he was working during the day. He was not able to leave his position; whereupon rabbit hair desensitization was instituted. This was successful until the patient received a maximum dose of 10 minims of 1:5,000 dilution every four weeks. He did not call at the clinic for three months, and when he did return an assistant inadvertently injected 10 minims of a 1:500 dilution. Within five minutes a general allergic shock was present; an acute asthma, accompanied by sneezing, rhinitis, conjunctivitis, general pruritis, and angioneurotic edema. Adrenalin was administered three times at half-hour intervals, after which the patient felt better and returned home. Several hours later he was admitted to the hospital with all the above symptoms exaggerated. In spite of heroic measures, his attack of status asthmaticus continued without remission for three days. He lapsed into unconsciousness on the fourth day and died.

The following detailed case report illustrates status asthmaticus of bacterial allergy, with recovery.

CASE 2.—Mrs. C., a teacher and school superintendent, forty-eight years old, weight 200 pounds, was admitted to the hospital on July 19,

*Read before the Twelfth Annual Meeting of the Association for the Study of Allergy, Cleveland, June 12, 1934.

1932, after having been ill one month with frequent attacks of asthma. She had been well until 1926 except for influenza in 1915. In April, 1926 (patient forty-two years old), she had contracted a cold, with severe laryngitis and complete aphonia which lasted two months. While under treatment for this, she had developed an attack of asthma which was relieved by adrenalin. In September and December, 1926, she had attacks of asthma which could not be relieved with adrenalin. She spent the winter of 1927 in Florida. Her laryngitis improved, but she had several attacks of asthma. In April, 1927, I first examined her, and at that time she had a capillary bronchitis, together with asthma.

X-ray examination of the chest and sinuses did not reveal any pathologic changes. Urinalysis and blood chemistry were within normal limits. She had no symptoms of the upper respiratory system, i.e., no nasal obstruction, sneezing, or rhinitis.

The patient was tested by the dermal method. A year later she underwent a complete retesting by the intradermal method. From 90 tests in each case she showed marked skin reactions to house dust and to various respiratory bacteria.

She received successful treatment with autogenous vaccine and with house dust extract. She remained quite well, visiting the office two or three times a year, until January, 1932. It was evident that we were dealing with an infectious form of bronchial asthma; for when she would visit me, she had attacks of laryngitis and bronchitis, followed by asthma.

Beginning in January, 1932, she had a continuous series of chest colds, until March. In June she was confined to bed with frequent attacks of asthma and bronchitis until her admission to the hospital in July, 1932. She had been told by her family physician that she was highly sensitive to morphine and to adrenalin preparations, both of which aggravated her condition.

On admission, July 19, 1932, physical examination revealed the ordinary findings of bronchial asthma, marked wheezing, numerous scattered râles, emphysema, etc. Pulse was 90, temperature 99° F., respiration 26, blood pressure 120/70 mm.

The patient responded to symptomatic medication and soon was comfortable. Four days after admission her temperature rose to 100°, the following day to 101°; there was an exacerbation of acute bronchitis, marked coughing, profuse expectoration, with a return of asthmatic attacks. Small doses of three to five minims of adrenalin alternating with ten minims of ephedrine sulphate were administered at two- or three-hour intervals in conjunction with other symptomatic treatment.

On July 26, the seventh day after admission, the temperature and pulse were almost normal, but subsequent to this, the patient began to show the following progressive and alarming symptoms: constant dyspnea to the point of exhaustion, constant wheezing, cyanosis, uncon-

trollable restlessness, jumpy and jerky movements of all extremities (day and night nurses were needed to keep the patient from falling out of bed), increasing irrationality, a low-muttering type of delirium, and periods of unconsciousness. Oral medication became difficult because of constant nausea and vomiting, with severe abdominal pains. On the evening of the fourth day of status asthmaticus we were confronted with an uncontrollable patient.

On July 28, the fourth day of status asthmaticus, the consensus of opinion differed as to whether she were dying a cardiac, a respiratory, or a muscle-nerve exhaustion death.

The following medications were administered ineffectually: liquor potassium citrate, codeine sulphate, aconite, bromides, phenobarbital sodium (gr. ¼ at frequent intervals), calcium gluconate (10 c.c. intramuscularly, daily), adrenalin and ephedrine (small repeated doses), anesthesine and cocaine, glucose (intravenously, daily), oxygen tent (for three days).

At midnight on July 28, 1932, two grains of phenobarbital sodium were given (by hypodermic) and repeated in two hours. In the morning the patient showed signs of improvement and became more comfortable. Two-grain doses of phenobarbital sodium were continued for three days several times each day. After that she was given symptomatic treatment and tonics, and in several days her pulse, temperature, and respiration had returned to normal. The patient was discharged on August 8, 1932, and returned to her family physician.

From the two cases reported here, and from others I have seen, I have been led to believe that some, if not all, of the following factors may be involved in the production of status asthmaticus: (1) There may be an overdose of the allergen (actopic reagin) to the shock tissues of the lungs. (2) There may be a simultaneous multiple involvement of shock tissue. The combined allergic shock from several sources is so great that the body cannot recover from the induced effect. (3) An idiosyncrasy may be present to the drugs used, that is, an exaggerated or retarded physiologic response, making it extremely difficult to judge the optimum dose. (4) There is a possibility of an added allergic shock in regard to a sensitivity to the drugs which ordinarily are beneficial.

In this instance strong sedation was extremely beneficial, and although symptoms disappeared too quickly, after heroic treatment, for a spontaneous remission to have occurred, yet we cannot rule this out.

DISCUSSION

DR. FRANCIS M. RACKEMANN.—I should like to begin the discussion by asking how many here have seen exactly the same kind of case. Will you hold up your hands?

[About twenty hands were raised.]

DR. RACKEMANN.—I ask that because I think maybe some day it might be wise to do what the pediatricians are doing, have a round table discussion, and such a topic as this would be quite desirable for that purpose.

There is one point I should like to make. As far as the course of asthma goes, the temperature chart does not help a whole lot, but every chart in every hospital has figures on the left, from one to ten and usually from one to twenty. If you will ask the nurse to record the number of times the patient needs adrenalin each day and then put a series of x's on the chart (it is not the total amount of adrenalin but the number of individual doses that is important) you will have a curve which goes up and down, and as the patient gets better, the adrenalin curve will come down to nothing. Then the chart will mean something.

DR. GEORGE PINESS, Los Angeles.—I should like to ask Dr. Sterling whether autopsy was done on his first case. In his second case the x-ray picture is typical of a group that most allergists have seen which is characteristic of a plugged bronchus and atelectasis. Both of the cases presented are typically those of acute bronchial asthma with a plugging of bronchi.

DR. MILTON B. COHEN, Cleveland.—These cases of status asthmaticus bother all of us. Some of them remind me very much of the type of very ill patients you see in the hospital when the medical wrecking crew goes around and everybody writes a note; particularly when the case cannot be well diagnosed or handled. If you go through the second, you find that somebody writes that the patient is a little bit improved, and some one else says he is a little bit improved; and the only thing you can figure out is that he died of improvement. I have had that happen to me a number of times in relation to these cases.

There is one point I should like to make. A number of times we have that type of patient in whom we could not demonstrate any specific cause, and we try to postulate something other than allergy that might explain the case. I showed some of these to Dr. Piness last February, and he said some might be early Ayerza's disease. Since then we have made a postmortem examination of one of those, and it shows exactly the same lesions as shown by Dr. Rowe, and that was in the case where the attack terminated within six weeks of inception. So these patients begin at least as true allergic cases and usually die of allergic obstruction of the bronchial tree, and we have not sufficient knowledge to find the cause and to remove it.

DR. BEN RAPPAPORT, Chicago.—I have found it useful to consult chemists when there are problems of this nature, and I have sometimes had considerable help. The last case of that nature was a patient of mine who was exposed to cat hair, to which she was extremely sensitive. She developed a status asthmaticus with vomiting as a persistent and prominent symptom.

I consulted Dr. Welker, head of the Department of Biochemistry at the University of Illinois. He wagered that because of the persistent vomiting a hypochloremia had developed and was aggravating the condition.

He was correct. The basal blood chlorides were around 200, and chlorides were administered. The patient was in an oxygen room. It was suggested later that possibly carbon dioxide in addition to the oxygen would have been good therapy, but the addition of chlorides subcutaneously was very beneficial, and nothing else was used in addition to the epinephrine. In twenty-four hours the condition cleared up. Whether the chlorides helped or not, there was certainly a definite hypochloremia which improved. That could have been due to the frequent vomiting which occurred in this case, and in almost all cases of this type.

DR. RACKEMANN.—What concentration of chloride did you inject, normal salt solution?

DR. RAPPAPORT.—Subcutaneously normal salt solution, and rectally a 5 per cent solution, without any glucose, because the addition of glucose to the chlorides merely delays absorption of the chlorides.

DR. HORACE BALDWIN, New York.—The only point I wish to bring up is one of rather speculative interest to me, and that is that among the seven asthmatic persons I have seen die in the asthmatic state, my impression is that a fairly good number of them had histories characterized by outstanding symptoms of neurasthenia and psychosthenia, emotional shock, and worry, previous to the onset of their status asthmaticus that went into final fatal termination. I wonder in the discussion that we had here today that there has been so little emphasis on the possible rôle of the autonomic nervous system in death from status asthmaticus.

DR. ALBERT H. ROWE, Oakland, Calif.—I have had an interesting experience which might be well to relate. I had a patient several months ago who was in a very severe state of asthmatic collapse, and as a last resort, according to the suggestions of Maytum, anesthesia with the colonic administration of ether in oil was induced. The patient was in severe collapse, but quieted down for a number of hours afterward. The following morning she awoke quite relaxed, expectorated a great deal of mucus during the day, and with the ordinary measures I was using before, she gradually recovered. It was interesting that I found a great deal of focal infection in this patient. Many teeth were extracted and at the present time she has made a very satisfactory recovery and is taking only one small dose of adrenalin a day. I believe that Maytum's suggestion for the control of severe intractable asthma is of value, and must be kept in mind for the desperate cases of this type.

DR. HARRY L. ALEXANDER, St. Louis.—I should like to inquire of Dr. Rappaport why he would be willing to bet he had a hypochloremia.

DR. RAPPAPORT.—You would not expect edema to develop in acute hypochloremia. It develops in postoperative patients very frequently, and there is no edema except when it has lasted for a considerable time.

DR. ALEXANDER.—What did that have to do with the asthma?

DR. RAPPAPORT.—I do not mean to imply that the hypochloremia causes asthma. It is merely symptomatic treatment. To have a hypochloremia in the presence of asthma merely aggravates the symptoms.

DR. HARRY S. BERNTON, Washington, D. C.—I think Dr. Sterling has done well to call the interesting facts to our attention, particularly the matter of therapy. He said something about oxygen. I wish you would take a vote and find out how many men use oxygen in cases of this character and how many men think well of the procedure.

DR. CHARLES H. EYERMANN, St. Louis.—In cases of status asthmaticus, I mean those individuals who have constant dyspnea requiring many doses of adrenalin during twenty-four hours, the underlying physical condition is acute pulmonary dilatation. They will be short of breath on account of emotional reactions or mere moving about in bed. Adrenalin, while helpful, is not the medication which will bring about the best results. Those cases should be treated with sedation.

DR. JONATHAN FORMAN, Columbus.—At a meeting of the Ohio State Medical Association in 1856, a paper was read on administration of ether for treatment of status asthmaticus.

DR. LEON UNGER, CHICAGO.—We had a girl twenty-four years old, with severe, intractable asthma, with many positive tests, but we never could relieve her by specific medication. She was in the hospital for a long time and had such terrific asthma, with such poor results in treatment, that the interne tried some sodium amytal intravenously and obtained a wonderful result, and the patient quieted down. One week later the asthma returned, so severely that a second injection of sodium amytal was given, with complete relief for another week. The third injection was given one week later for a recurrence, and while the needle was still in the vein, the patient died. No autopsy was obtained.

DR. ROBERT WARD LAMSON, Los Angeles.—I have seen several patients in a condition of status asthmaticus who did not respond favorably to epinephrine, and a few of these had been given morphine with resulting detriment. The use of caffeine sodium benzoate 7.5 grain ampules, repeated every fifteen minutes for four doses if necessary, has given definite relief. If the patient's condition is not too serious, caffeine citrate in 5 to 7 grain doses, by mouth, may be effective. In fact, certain patients respond to this drug better than to epinephrine. It has one definite disadvantage, namely, the possibility of producing considerable gastric discomfort.

DR. HAL DAVISON, Atlanta.—Some years ago in attempting to relieve a bad case of asthma, I had administered to the patient 75 minims of adrenalin over 1 grain of morphine, some chloretone, chloralhydrate and codein. By this time I felt I needed some consultation. The physician called suggested the administration of apomorphine; the patient was given $\frac{1}{60}$ grain and was asleep in three minutes. Up to this time I had been somewhat afraid of apomorphine because of a reaction I had seen in a patient when I was an interne. Following this time I experimented with the use of apomorphine and found that a combination of $\frac{1}{120}$ to $\frac{1}{100}$ grain apomorphine with 1 to 2 grains codeine and 8 to 10 minims of adrenalin made up together and one-third of this administered every five to ten minutes until the whole was given would, in practically every case, stop a severe attack of asthma. In cases that have not responded to this treatment we have used ether in oil by rectum.

DR. GRAFTON TYLER BROWN, Washington, D. C.—Some patients with status asthmaticus, although not so severe as those Dr. Sterling reports, seem to have been definitely benefited by 31 grains of sodium iodide intravenously. Also, when a patient has had no rest and seems completely exhausted, I have resorted to morphine and atropine, and inside of fifteen minutes he is usually relaxed and breathing quietly. I consider morphine a life-saving measure in some of these cases, although I fully appreciate the contraindications to its use in asthma. When morphine is necessary, I usually administer it in adrenalin, to slow the absorption and to offset the depressing effect.

DR. OSCAR SWINEFORD, JR., University, Va.—I did not mean to joke about the use of whisky in status asthmaticus. Dr. Duke has recommended it, and I have had two patients in the past twelve months to whom I have given as much as 150 minims of adrenalin in twenty-four hours without appreciable relief. But when I administered three ounces of whisky they were relieved within ten or fifteen minutes. I found that they could be kept relaxed and quite comfortable for periods of several days by two- or three-ounce doses of whisky several times a day.

DR. STERLING.—I am not in favor of the oxygen tent. I have used it with unsatisfactory results in half a dozen cases. I did not mention all the drugs used in the last case. Besides those mentioned, we used suppositories of 15 grains chloralhydrate and 30 grains sodium bromide in cocoa butter, without any effect on several occasions. I have tried some of the other remedies suggested with unsatisfactory results. Whisky was also used in this case, but it did not do much good.

Society Proceedings

THE ASSOCIATION FOR THE STUDY OF ALLERGY

TWELFTH ANNUAL MEETING, CLEVELAND, OHIO, JUNE 11 AND 12, 1934

The Phases of Foreign Protein Sensitization in Human Beings.* T. DUCKETT JONES AND JOHN R. MOTE, Boston. (Abstract.)

During the course of a series of skin tests on human beings with streptococcal material which contained a minute amount of rabbit protein, a group of seventy individuals were sensitized to varying degrees with rabbit protein.

The first evidence of sensitivity to this protein was a delayed twenty-four-hour type of skin reaction. Following this, the same individuals, after repeated tests, developed the usual immediate wheal and flare of serum protein sensitivity. In addition, there was noted a five- to eleven-day delayed type of reaction, which occurred locally at the site of injection of 0.01 c.c. of rabbit serum.

Approximately eight months later the majority of these individuals were retested for evidence of residual sensitivity to rabbit protein. It was found that there was a great individual variation in the ease with which sensitivity was lost. The sensitivity decreased in the reverse order of its appearance. Some individuals maintained their immediate wheal sensitivity. Others who had previously had the immediate wheal, after an interval of eight months, had only a delayed twenty-four-hour type of reaction; and some had become completely skin negative.

In a quantitative study of the degrees of sensitivity, none of the twenty-four-hour skin reactions were transferable by the Prausnitz-Küstner technic. The sensitivity was transferable in 5 of 14 individuals in whom it was attempted, during the immediate wheal stage of sensitivity. This was noted in two instances at least eight months after the development of the immediate wheal.

Two individuals had demonstrable precipitins, and in both instances the sensitivity was transferred locally to guinea pig skin by the Ramsdell technic. In no instance was the sensitivity successfully passively transferred to the guinea pig.

The ease with which human beings may be sensitized by minute amounts of foreign protein is demonstrated. A delayed twenty-four-hour type of skin reaction, under such conditions, is the first evidence of sensitivity. This progresses to the usual immediate wheal type of reaction of foreign protein sensitivity.

*From the House of the Good Samaritan, Boston, Mass. The expenses of this study have been defrayed by a grant from the Commonwealth Fund.

DISCUSSION

DR. FRANCIS M. RACKEMANN, Boston.—I should have told you a little about Dr. Jones when I introduced him. He is a student of rheumatic fever, and he is a good student, and that is the reason why he observed these reactions as a sort of by-product to his other studies. He has presented his work before, and I asked him to come here because I wanted you to see at first hand what he has been doing. To my mind his work is quite fundamental and important.

There is one question about it, however, which is interesting, and that is whether these reactions artificially produced in animals and man are quite the same as the other reactions which occur spontaneously in allergic individuals.

Dr. Jones has actually produced a general reaction in a patient who, I understand, was artificially sensitized, and in other patients he has observed the presence of circulating antibodies, not only in the form of Prausnitz-Küstner bodies, but also in the form of precipitins. This is important, and I would ask Dr. Jones to say a word about the clinical histories or make-up of those patients, especially of the one who showed the general reaction, and of the others who had precipitins.

DR. LOUIS TUFT, Philadelphia.—In 1930, I reported upon a similar phenomenon, in the course of experiments published under the title "The Skin as an Immunologic Organ." In these experiments horse serum was used as a sensitizing agent.

In the course of experiments demonstrating the presence of reagins in serum sickness, I found that individuals who were being used for passive transfer, and who were negative initially to horse serum by skin test, after an interval of ten days or two weeks would show positive skin reactions to horse serum upon being retested. In one of these subjects we demonstrated the reagins by passive transfer in the serum.

This and other experiments reported in the same article emphasized the importance of the skin as an immunizing and as a sensitizing organ. These experiments are similar to what Dr. Jones and Dr. Mote have reported here except that rabbit serum was used in this instance as the sensitizing agent.

From a clinical standpoint I should like to ask any of the members of the audience, as well as the authors, whether they have had similar experiences with agents used as ordinary allergens, and particularly with milk protein. About ten years ago I administered "Aolan" intradermally for purposes of nonspecific therapy; about ten days later after the third injection there developed an immediate large local reaction and some constitutional manifestations.

I did not recognize this at the time as being allergic in character. Two days later the patient was given another injection of a similar type by another physician. Following this he passed into a state of shock from which he was easily revived. I did not skin test him to milk protein because he never returned for treatment, but I do not doubt that the symptoms were due to an acquired sensitiveness. I wonder whether in the administration of milk as a protein there are not many more instances of such sensitization than we are accustomed to believe.

DR. WARREN T. VAUGHAN, Richmond.—I think this work is very fundamental. Probably sensitization would be much easier to produce

in human beings if, instead of working with things that human beings are usually coming in contact with, we used substances with which human beings rarely come in contact. Rabbit serum and guinea pig serum, and those things which are being used by Dr. Jones and Dr. Simon, are such substances. It seems to me to bring allergy and anaphylaxis much more closely together.

I have found that in individuals who were only mildly allergic, whom we call the minor allergics, almost without exception the foods to which they have become sensitive are the foods eaten only occasionally rather than those which are eaten constantly.

I should like to ask Dr. Jones whether he has tried feeding rabbit meat to any of these patients and with what results.

Dr. Bret Ratner, New York.—It is very gratifying indeed to see the marked change that is coming about in our comprehension of the allergic problem. I think we all know that there has been a group of men, pioneers in this work, who, it seems to me, have emphasized the heredity aspects of allergy too strongly, and it is rather interesting to read a book written by Ryan, in 1793, in which he decries the fact that the physicians of that time, because of their lack of knowledge on the subject of asthma invoked the hereditary theory.

The work that has been so clearly presented by Dr. Jones indicates that probably the most important factor in establishing a state of hypersensitiveness is quantity.

The reason all individuals do not become sensitized, it seems to me, is that they have escaped getting a huge amount of a particular antigen at one particular time.

The next illuminating fact that Dr. Jones brought out is the evanescent character of the Prausnitz-Küstner antibody, and the precipitin. We know that in human experimentation the same thing obtains, for some work that we have been engaged in shows rather conclusively that the Prausnitz-Küstner antibody may be in the blood stream at certain times and not at others.

I was very happy indeed to hear Dr. Jones's presentation of that very same fact.

Dr. Frank A. Simon, Boston.—We have done some work with the injection of guinea pig serum into human skin, and, contrary to what you might think, both normal persons and those with hay fever and asthma could be sensitized with equal facility. A small quantity, that is, a few tenths of a cubic centimeter of a 1:1,000 dilution is sufficient for many normal or atopic persons, and if a larger dose is used (1:100 or 1:10 dilution) everybody becomes sensitized.

An interesting finding is that we are unable to sensitize anybody to egg white or cow's milk. We thought one reason might be that these people having had previous contact with hen's egg and cow's milk might have become sensitized and desensitized, and hence refractory to further sensitization, and so we obtained some turtle eggs and mare's milk, and we found that even though large doses were injected, no one became sensitive to turtle's egg or mare's milk.

You can put as much as 0.5 c.c. of undiluted egg white into the human skin, and it does not produce hypersensitiveness, as determined by intradermal test, and yet we know hypersensitiveness to egg white occurs naturally. The reason for this discrepancy is unknown. It illus-

trates again the difference between atopic or naturally acquired hypersensitiveness and the anaphylactic or artificially acquired type.

DR. ARTHUR F. COCA, New York.—The experiments that have just been described are like those that have been reported by others. In fact, there are several substances besides those mentioned today which are known to stimulate reagin production in nonallergic persons.

Ascaris protein is a very good reagin-producing antigen. Many persons—I will not say all, but a great majority of persons—in contact naturally or by injection with ascaris, produce reagins. Dr. Tuft has spoken already of horse serum. There is also insulin, and now we have rabbit and also guinea pig serum protein.

Dr. Brunner carried out some experiments, which are illuminating, in the injection of various antigenic substances, including egg and orris, into persons who have inherited allergy. I have been calling this "atopy," and others also use this convenient term.

Brunner succeeded in one instance in inducing anti-orris reagins, which, however, were demonstrable only during a brief period (a few months).

When Brunner produced reagins for orris in the atopic person, who suffered from natural atopic symptoms, this person during the period in which the reagins were present had an attack on natural contact with orris.

This would seem to bring atopy closer to anaphylaxis but it does not. It tends rather to emphasize the importance of the constitutional hereditary character, which, I think, has been very clearly and acceptably demonstrated.

The difference is this: Induced reagin production is characteristically short lived. Anti-ascaris reagin production is longer, but that, too, is relatively short lived.

On the other hand, the *natural* reagin production in the atopic person is, as we know, typically long lived, often persisting throughout the life of the individual.

It seems to me that this distinction ought to carry considerable weight in support of the already strong evidence of the existence and importance of the constitutional character.

DR. JONES.—In answer to Dr. Rackemann's question concerning the allergic clinical history in these patients, I may say that the patient showing a generalized reaction presented a story of being sensitive to eggs. So far as we could determine, there were no further sensitivities among the other 69 patients. The patient developing precipitins, in addition to the previously mentioned patient, was not known to be sensitive to any protein or allergen.

I appreciate Dr. Tuft's remarks highly. No attempt was made to give any extensive review of the literature, and the pertinent work of many observers present could not be reviewed. The work of Tuft and Ramsdell on immune and normal horse serum was quite comparable to a goodly part of the work presented.

Dr. Vaughan's suggestion concerning the use of proteins with which human beings rarely come in contact, is a pertinent one. Dr. Simon has mentioned that this work as presented is a by-product of other studies, and since rabbit protein was present in the material used, it was decided that the experiment be completed with this material. Its repetition

with other proteins is being contemplated. The feeding of rabbit meat to these patients was considered but abandoned, in view of the possibility of reactions which might be unpleasant and possibly dangerous.

It was very kind of Dr. Coca to discuss this work. It was not my purpose—nor am I qualified—to discuss at length the theories and hypotheses concerning allergy and anaphylaxis.

I did wish to present an interesting series of events which may add to our conception of these important phenomena. In doing so, I wish only to observe and record. It is evident that the majority of individuals receiving any appreciable number of injections become sensitive. It is also true that there is a great variation in the ease with which these individuals become sensitive, and the allergically alert ones will react more quickly, and also will maintain their sensitivity for a longer period of time than the average.

I think that in addition to the possible light that this may throw upon some fundamental features of the various sensitization phenomena, it suggests decidely that we must further study bacterial allergy and determine just what the twenty-four-hour type of reaction to bacterial products may mean. This we hope to do in the near future.

Eosinophilia in Syphilis. RALPH H. SPANGLER, Philadelphia. (Abstract.)

The occasional finding of an eosinophilia (5 per cent to 10 per cent and at times higher) in a patient with no allergic manifestations, who gave a negative luetic history and had no clinical symptoms of syphilis, but whose blood Wassermann reaction subsequently proved positive, has interested me for a number of years. A recent connection with the Medical Service of the Philadelphia County Prison with its vast amount of clinical material, among a yearly turnover of 30,000 men, offered the opportunity to make a comparative study of the differential leucocyte counts in 100 positive and 100 negative blood Wassermann cases.

The literature on the whole is rather indefinite when one reviews the reported data on "blood findings in syphilis." Certainly no typical or specific morphologic blood picture in syphilis is recognized or has been established, and from reports at hand the leucocytes in syphilitic infection seem not to have received nearly so comprehensive investigation as have the red cells. I have found no report recording a series of differential leucocyte counts in syphilis, and the findings in the present series of 100 positive Wassermann cases appear to be unique so far as it has been possible to correlate them with the available reports furnished by the literature.

Our method of investigation was briefly as follows: Differential leucocyte counts were made on 21 men with positive Wassermann reactions who had *primary lesions* and on 9 men who had *secondary lesions* (skin manifestations)—30 cases. Then, coincident with routine taking of blood for Wassermann tests, in prisoners assigned to certain work, blood smears were made until we had accumulated 70 additional differential counts (making a total of 100) on men whose blood Wassermann re-

actions were positive, and 100 differential counts on men whose Wassermann tests were negative.

HEMATOLOGIC SUMMARY

In the series of 100 men with positive blood Wassermann reactions, the differential leucocyte counts show:

40% with an eosinophilia	Eosinophiles	5% to 10%
74% with a lymphocythemia (combined large and small)	Lymphocytes	26% to 50%
10% with a neutrophilia	Polymorphonuclears	76% to 89%

In the series of 100 men with negative blood Wassermann reactions, the differential leucocyte counts show:

4% with an eosinophilia	Eosinophiles	5% to 6%
68% with a lymphocythemia (combined large and small)	Lymphocytes	26% to 53%
16% with a neutrophilia	Polymorphonuclears	76% to 87%

CLINICAL ANALYSIS

For a more detailed clinical analysis and comparison the differential leucocyte counts in the series of 100 positive Wassermann cases are separated into four groups, which summarized reveal the following:

Group I, 21 Men With Initial Lesions

Nine (42.85%) show an eosinophilia	Eosinophiles	5% to 10%
Thirteen (61.90%) show a lymphocythemia	Lymphocytes	26% to 48%
Four (19.04%) show a neutrophilia	Polymorphonuclears	76% to 85%

Group II, 9 Men With Secondary (Skin) Manifestations

Four (44.44%) show an eosinophilia	Eosinophiles	5% to 6%
Seven (77.77%) show a lymphocythemia	Lymphocytes	26% to 45%
None show a neutrophilia	Polymorphonuclears	under 75%

Group III, 47 Men Who Never Had Received Treatment and Who Did Not Know That Their Blood Wassermann Reaction Was Positive

Twenty-one (44.68%) show an eosinophilia	Eosinophiles	5% to 9%
Thirty-five (74.44%) show a lymphocythemia	Lymphocytes	26% to 50%
Three (6.38%) show a neutrophilia	Polymorphonuclears	76% to 83%

Group IV, 23 Men Who Had Received Previous Intravenous Treatment

Six (26.08%) show an eosinophilia	Eosinophiles	5% to 7%
Nineteen (82.60%) show a lymphocythemia	Lymphocytes	26% to 40%
Three (13.04%) show a neutrophilia	Polymorphonuclears	76% to 89%

No men with a history of the commonly recognized allergic diseases were included in either the positive or the negative series, but the negative men could not all be classified as normal subjects, since a few had a cardiovascular or gastrointestinal disturbance and a number presented various neurotic manifestations with a physical basis in most instances for the symptoms.

Among positive Wassermann cases we encountered 3 cases of asthma, 4 of urticaria, and 1 case of exfoliative dermatitis with total white counts of 26,400, 12,000, and 19,600, showing respectively 37 per cent, 35 per cent and 38 per cent of eosinophiles.

Among negative Wassermann patients were encountered 2 cases of asthma, 2 of urticaria, 1 of psoriasis, and 4 of generalized pruritus. Among the negative Wassermann patients was also one who had eosinophile counts of 20 per cent, 25 per cent and 18 per cent respectively in the course of a month. Examination of his stools revealed the presence of *Trichuris trichiura*. His total white counts were 13,600, 15,200, and 10,200, the leucocytosis being of the polymorphonuclear type.

Wright's method of staining was used, and all counts were made by the same technician (Kolmer trained) in order to eliminate the factor of personal equation. It is realized that it would have made the investigation of more value to have included a total white count in each case and also to have counted from 200 to 400 cells instead of only 100 in each differential count, but the circumstances under which the work was done made such a procedure impossible.

Appreciating, however, the daily variability of blood counts in health and disease, and realizing that our findings with only one differential count of 100 cells each are not unalterable conclusions, but may be regarded as only suggestive, a more complete and intensive study was made on six strongly positive (plus 4) men, whose stools were negative for ova and parasites and who had received no previous medication. Eight differential counts were made in each case on separate days within a period of two weeks. These counts are tabulated in modified Schilling hemograms.

Summary of Hemogram Findings.—The hemograms illustrate the importance of making repeated counts on separate days if the occurrence of eosinophilia is not to be overlooked. In each hemogram from 2 to 8 of the counts showed the presence of 5 per cent to 15 per cent of eosinophile cells.

The hemograms also confirm the finding of a lymphocytosis in syphilis. The combined lymphocytes in each count being well above Howell's normal range of 20 per cent to 25 per cent, with a relative increase of the large lymphocytes—which are regarded by many hematologists as the younger forms of cell—hence a suggested Arneth shift to the left. The neutrophilic granular cells are uniformally below the normal range (60 per cent to 75 per cent), with the "young forms," the myelocytes and band cells, all within normal limits; hence there is no neutrophilic nuclear shift to the left. The large hyaline monocytes are within the normal range (2 per cent to 10 per cent), so that no evidence of a monocytosis was present in any of the counts.

The findings in this smaller group on the whole confirm and tend to emphasize that the suggested conclusions drawn from the series of 100

positive cases may be considered correct for the average. Moreover, the counting of 100 cells on eight different days is probably of more value in substantiating the periodic occurrence of a blood eosinophilia than would have resulted from the counting of 800 cells in two or three blood smears made the same day.

It seems fair to presume, therefore, that had we made repeated differential counts, instead of only one, in the series of 100 positive cases the percentage showing a periodic occurrence of eosinophilia would have been much higher, possibly nearly 100 per cent.

SUMMARY

The chief findings in the series of 100 differential blood counts on 100 nonallergic men with positive Wassermann reactions are:

1. Forty per cent showed an eosinophilia ranging from 5 per cent to 10 per cent.
2. In Group 3, men without clinical symptoms and who did not know they had positive blood Wassermanns, the percentage of cases showing an eosinophilia was as high (44.68 per cent) as that of the men with primary lesions (42.85 per cent) and as that of the men with secondary lesions (44.44 per cent).
3. Seventy-four per cent of the 100 positive cases showed a lymphocythemia with a relative increase of the large lymphocytes, confirming previous reports in the literature of a lymphocytosis in syphilis.

CONCLUSIONS

1. With the hypothesis that eosinophilia is a criterion of allergy, and with the finding of an eosinophilia in positive Wassermann individuals, in various stages of syphilitic infection, the possible immunologic relation of allergy and syphilis would appear to justify careful study.

2. With the admittedly high incidence of unrecognized syphilitic infection and the unknown basic factor of many allergic metabolic disturbances, any clue leading to a definite diagnosis, and that may aid in solving the mechanism involved in a systemic eosinophilogenic response would seem worthy of attention and investigation from an immunologic standpoint.

3. Finally it seems justifiable to conclude that a moderate degree of eosinophilia, especially when associated with a lymphocytosis, occurring even periodically in an apparently nonallergic individual whose intestinal tract is free from ova and parasites, warrants the taking of Wassermann tests and the making of a persistent search for clinical evidence of syphilis.

DISCUSSION

Dr. George Piness, Los Angeles.—Since the discussion of eosinophiles has come up time and time again for the past few years and particularly since the work of Dr. Hensel, who has called our attention to their im-

portance in the study of the allergic individual, I think that it is timely to suggest that instead of studying eosinophiles from the differential count, we make total counts similar to those when total leucocytes are counted. There is now available a solution which is applicable to such a study. This solution will blot out all other types of cells and make the eosinophiles stand out so that they may be counted. A preliminary report from one of my workers will appear in the *Journal of the American Medical Association* in the near future. The importance of this count in our experience has been that one can determine by it that part of the allergic cycle in which the patient is at the time of the count.

Rhinologic Method From the Standpoint of the Allergist. HORACE S. BALDWIN, NEW YORK. (Abstract.)

An attempt is made to stress the important interrelationship that should exist between the allergist and the rhinologist. Skillful and adequate handling of the nose and throat side of his work is of the utmost importance to the allergist in securing for his patient the best therapeutic results. It sometimes seems unfortunate that the terms "radical" and "conservative" have been used to denote the type of rhinologic surgery employed. It would seem better that adequate surgery with a knowledge of the allergic background should be the ideal.

It is often only too true that by conservative surgery is meant a method of *laissez faire* and too much reliance on the negative clinical examination without use of more delicate diagnostic procedures and too little insight into the allergic aspects of the case. This is particularly true in the hyperplastic infections of the mucous membranes where the infection is deeply embedded and in the too easily satisfied system of removing polyps without trying to correct the underlying disease. As a result many of these patients proceed to develop a chronic asthmatic state with continued increase in the infection in the lung itself that is almost impossible to eradicate even when eventually adequate surgery is arrived at. The same holds true for the policy of continued irrigation of antrums with infection buried in the mucous membrane or that are frankly polypoid. Timorous surgery that does not accomplish more than stirring up deeper infection had better not be done at all. Halfway surgery that clears up infected antrums and leaves other sinuses infected offers little hope of success. At the same time, to us as allergists, reliance on vaccines for the control of these conditions has little evidence to recommend it.

The term "radical surgery" has often seemed to be connected with extensive operations without adequate knowledge of the allergic factors involved in the presence of atopic inhalants in the air and of atopic foods in the diet. Also too often is surgery attempted with underlying disease in the lung, be it chronic bronchiectasis, emphysema or chronic bronchitis, which acts as a very definite deterrent to satisfactory results. We are often pessimistic when we see these patients with accessory nasal

sinus disease because the results often do not justify the effort and trouble involved in the attempt to clean out the infection thoroughly. However, it is felt that palliative nasal surgery has failed to secure satisfactory results. At present it would seem better to try to secure as near the perfect anatomic and surgical result as can possibly be obtained with full comprehension of the allergic background that exists.

DISCUSSION

DR. HARRY L. ALEXANDER, St. Louis.—As Dr. Rackemann remarked, this is very timely, because Dr. Baldwin, and perhaps correctly, informs us we should do a thoroughly extensive operation or none at all, and we do hesitate to do extensive operations on the nose.

I think it is interesting to hear a report on the rhinologic aspects of allergy without mention of eosinophiles. I bring it up because in the rhinologic journals more and more rhinologists are becoming allergically minded, if you will pardon that expression. They have learned to identify eosinophiles and their criterion of allergy is based very largely upon their ability to identify eosinophiles in the nose. The opinion that localized eosinophilia is a criterion of allergy has been altered a little by Dr. Cooke's observations last year, and others may feel that infectious as well as atopic allergy may induce a local eosinophilia. I think it is timely to discuss this in terms of the experience of those who are particularly interested in the subject. I should ask Dr. Baldwin whether he thinks a localized eosinophilia is a definite evidence of allergy as we understand it, or whether it may exist without allergic lesions.

DR. HARRY P. SCHENCK, Philadelphia.—I believe I should defend the rhinologist. It is gratifying to have this paper point out that in irrigation of an antrum the return of clear fluid does not imply that the sinus is negative. Most allergic patients, with clinical or roentgenologic abnormalities of the sinuses, will return clear irrigating fluid.

Another point I should like to make is that erroneous conclusions may be drawn concerning the rhinologist's care in examination, because the roentgenologist examines the patient two or three weeks after the clinical report has been made. This is unfair to the rhinologist because in this interval exposure to an allergen may produce tremendously thickened membrane in one or more sinuses. Clinical and roentgenologic examinations should be made the same day.

I feel that the average rhinologist is at the present time acutely aware of the possibilities of allergic changes in the upper respiratory tract, even to the point of obtaining too many skin tests. A patient who sneezes once is liable to be sent to the allergist for extensive and often futile study without seeking other evidence of sensitivity. Many patients sent to the rhinologist by the allergist require not rhinologic interference but adequate treatment by the allergist to prevent or arrest progressive changes in the nasal mucosa. For instance, many mucous polyps will disappear with adequate allergy measures alone. Disappearance of polyps under such circumstances has been noted in Germany and France as well as in this country, so that I believe there is little doubt that some mucous polyps disappear following desensitization.

Dr. Alexander has mentioned the varying significance of eosinophiles, and I also wish to emphasize that the alterations in the nasal mucosa,

resulting from allergy, whether termed hyperplastic rhinitis or otherwise, do not continuously show the presence of eosinophiles. Eosinophiles are frequently present during exposure to an allergen but not always during a long period of freedom from exposure. Nasal mucous polyps likewise may lose their eosinophile content if the patient loses contact with the allergen that has been responsible for the tissue changes.

DR. FRENCH K. HANSEL, St. Louis.—In the management of patients who have hyperplastic sinus disease or polyposis associated with or without asthma, it has been our experience that each case presents an individual problem for solution. In the first place, we believe that the allergic factors are of primary importance, and that results are dependent upon their control. In the evaluation of pathologic changes in these cases, the question frequently arises as to the possible existence of acute or chronic infection. If a patient is examined during the subacute stage of an acute infection, an abundance of mucopus will be observed, and one's first impression under such conditions would be that perhaps a chronic pansinusitis exists. These patients should be observed over a period of many weeks in order to determine definitely whether infection is acute, subacute, or chronic.

The cytologic findings in the secretion must be correlated with all the other clinical facts. It has been our experience that a pure eosinophilic response is an indication of allergic reactions. In the presence of acute or chronic infection, there is a marked neutrophilic response, and many pus cells are seen in the secretion. By making repeated examinations of the nasal and paranasal sinus secretions and determining the relative proportions of eosinophiles and neutrophiles, a fairly reliable index of the pathologic process occurring in the tissue may be obtained.

It has often been our experience that in a great many cases of polyposis repeated acute infections occurred as long as the allergic reactions were not controlled. If nasal polyps are removed before allergic reactions are under control, there is a tendency to rapid recurrence. With the subsidence of allergic reactions, not only is there a decrease in the susceptibility of the patient to infection, but the nose and sinuses are better prepared for surgical interference.

Every case, therefore, is an individual problem which may be solved only after repeated observations and the correlation of all of the facts assembled from the clinical history and laboratory findings.

DR. GEORGE PINESS, Los Angeles.—Dr. Baldwin's paper is somewhat misleading from the standpoint of the title of his presentation. I have always felt that regardless of whether an individual has an allergic condition with a complicating sinusitis or other pathologic condition in the nose, these complicating factors should they require surgical procedure should be cared for and considered a separate entity from that of the allergy. It is a mistake and one is usually in error to tell such individuals that surgery will relieve or cure the underlying allergic condition. Men who were enthusiastic about their results procured by radical procedures have become more conservative and do not claim too much for radical surgery. In my own experience over many years in the field of allergy I have yet to see a single case where radical or conservative surgery has given any allergic individual permanent relief. It is true that removal of tonsils or other surgical measures give relief for a short period of time, but without exception there has been a recurrence of the allergic condition for which he first consulted the physician. One

should be most guarded in referring patients to consultants who are radical in their procedures and who offer great promise of relieving or curing allergic individuals of this condition.

DR. CHARLES N. HENSEL, St. Paul.—I cannot let that statement of my friend, Dr. Piness, go unchallenged. I have maintained my interest in allergy and have applied allergy as a necessary adjunct to my work in internal medicine. Therefore, I consider a patient from his whole constitution, while the individual confining himself exclusively to the practice of allergy tends to think of the patient exclusively from the allergic point of view.

My own experience has shown me definitely that there is a middle ground between extreme points of view. We have to admit that the allergic individual has some constitutional defect, but we would not refuse to allow such an allergic individual to have the benefit of the removal of a gangrenous appendix, and likewise I see no reason why we should refuse to let the allergic individual have the necessary surgical drainage to relieve infection in the sinuses. I am confident that many situations are in the nature of double-headers, namely, that we have both allergic manifestation and infective manifestation. In some cases it is the infection that is the trigger to set off the attacks, and in others it is the allergy that sets off the attacks.

I have a theory that noxious allergens circulating in the blood which flows to the mucous membranes lining the sinuses irritate this delicate mucous membrane—lower its resistance and make it more prone to the insult of infection. If drainage is free, the elimination of the offending allergens from the blood will allow these irritated nasal tissues to return to normal, but if nasal drainage is obstructed, then even though the offending allergens are removed, the infection persists and must be dealt with as any infection.

I have recently seen some work on the relationship between asthma and sinusitis presented by a very good rhinologist in my district, in which he made, under the microscope, a very nice differentiation between the mucous membrane from the purely infectious type and the mucous membrane from the allergic type. In the infectious type there was some thickening of the mucosa, but there was a marked fibrous thickening of the submucosa with leucocytic infiltration; whereas in the allergic type there was a marked thickening of the mucosa and a very large increase in the size of the goblet cells.

From the foregoing, I believe we should be cautious in accepting such a statement as has been made, namely, that any permanent results from rhinologic treatment in an allergic individual has not been seen.

Dr. Piness speaks from the background of a very large clinical experience, but living as he does where furnace heat is not so necessary, which in so many domiciles results in atmospheric air that is woefully lacking in moisture, which condition prevails through six or seven months of every year, he does not see the same type of infectious sinusitis that we do in the northern states. In my part of the country, patients begin to have attacks of sinusitis as soon as the windows are closed and the furnace heat is turned on, when the cold weather arrives, and from my experience, unless we deal with the infectious element in these cases and provide drainage, we do not get completely satisfactory results.

DR. PINESS.—I should like to correct Dr. Hensel, since his discussion gives an erroneous impression of what I actually said. I have always

contended that if a patient has a complicating sinusitis or infection of any of the accessory sinuses it should be taken care of by the rhinologist as a separate and distinct entity without considering the allergic condition present. I also made the statement that in my entire experience I never have seen a single individual who received permanency of relief from his allergic condition by operative procedures on his nose and throat.

DR. J. A. RUDOLPH, Cleveland.—I think that the remarks Dr. Hansel, of St. Louis, made, were very pertinent, and I believe had his remarks been closely and carefully listened to, some of this discussion might have been unnecessary. He mentioned that every problem in nasal allergy of the type under discussion should be individualized, and I believe that one cannot overemphasize that statement. I think that each patient who comes into your office with a nasal allergy must be studied from the standpoint of the rhinologic problem as well as from the standpoint of the allergic problem.

I believe that one cannot separate the field of medicine into the right nostril specialist and the left nostril specialist, and the right leg specialist and the left leg specialist. We must not forget that we are physicians as well as allergists.

We have been especially interested in the nose of negative skin test patients with nasal allergy. How could one study them from any standpoint if the methods we have at present are inadequate? We did not obtain positive reactions by the scratch nor by intradermal technic.

There are additional methods that have to be devised if such cases are to be diagnosed and treated, and men in the field of rhinology are perhaps better able to assist us if they understand the problems in allergy. This point I should like to emphasize: if it is necessary to study a patient from the rhinologic aspect, then as allergists we must let a rhinologist who understands allergy study the problem with us, for it is only by the most complete cooperation that this type of medical problem can be solved.

DR. BALDWIN.—Concerning the question of eosinophilic cells, that Dr. Alexander brought up, my feeling has been that eosinophiles in the nose do not necessarily indicate inhalant sensitivity or food sensitivity; they are also found associated with very definite bacterial infection in these cases of asthma.

Concerning what Dr. Piness has had to say, I am of the belief that a great many of our modes of therapy in allergic conditions are not curative. However, it has been our experience that where nose and throat pathologic conditions were demonstrated and could be favorably influenced by surgery, enough relief was brought to the patient to justify it.

I do not intend to lead any one to believe that I think every patient with infectious asthma should have a Caldwell-Luc operation and an ethmoidectomy done, but I do think that there are numerous individual cases where these measures are definitely indicated after thorough study of the individual case. Some patients may have to be treated conservatively, but there is no good reason, in my experience, why we should not, where it is possible, try to eliminate the infection by means of the more severe operative procedures instead of merely making gestures with packs and tampons.

I am in entire agreement with what Dr. Rudolph has said.

Department of Reviews and Abstracts

Selected Abstracts

The Levels of Serum Calcium During an Asthmatic Crisis. Drilhon, A.: Compt. rend. Soc. de biol. **115**: 23, 1934.

Struck by the abnormal quantity of calcium eliminated in the urine in certain asthmatic subjects, the author has been led to try, with a technic as precise as possible, to determine the blood calcium in these patients.

The station at Mont-Doré furnishes the author a number of patients, so that he has been able to test 115 well-defined cases of which 40 patients had a particularly severe crisis. He found the values of blood calcium high in these instances. He then transferred his researches to Paris, on a patient with extremely acute asthma. He obtained blood during periods of paroxysms and confirmed his previous experience, and obtained the following values, namely 250 mg., 280 mg., and 260 mg. of calcium per liter of serum.

In the light of these experiments, the author concluded that an asthmatic during his crisis shows a marked hypercalcemia. He used the technic of Guillaumin on the serum, separating it as quickly as possible from the clot. When applied to normal individuals this method in his hands gave results varying between 94 mg. and 160 mg. per liter.

According to his knowledge, no previous authors had deliberately investigated as he has calcium values during a crisis, which would explain the difference between previous results and his in asthmatic individuals.

Intravenous Injections of Hypertonic Magnesium for Migraine. Lumiere, A., and Meyer, P.: Compt. rend. Soc. de biol. **115**: 534, 1934.

These authors have for a long time called attention to abnormalities in the colloidal state of the blood during various forms of allergy. Certain clinical expressions of allergy, such as asthma, dermatoses, etc., have been treated successfully by the intravenous injections of the hyposulphite of magnesium in solutions of 10 per cent to 25 per cent or 50 per cent.

The administration must be done very cautiously. The total dose of 5 c.c. must be injected in successive fractions intravenously. One begins with 1 c.c., which is followed immediately by a feeling of warmth which lasts less than a minute. When this has disappeared. another 1 c.c. is injected, and the injections are thus given until the total dose has been administered. When this technic is followed, there is no danger.

Among the patients was a woman who had suffered for thirty-five years with almost permanent migraine, which disappeared almost immediately after injection. One could determine also a diminution of the colloidal osmotic pressure of the blood and a raising of the chlorides. Other cases of migraine have been similarly successfully treated.

Sensitization Tests: Their Value in Dermatology. Mendelsohn, H. V.: Arch. Dermat. & Syph. **29**: 845, 1934.

A series of 262 cases of various dermatoses was studied over a period of four years by a group of four men well acquainted with the theoretical and practical phases of immunology. The dermatoses included eczema, urticaria and dermatitis venenata (80 per cent of the cases), and also prurigo, erythema multiforme, angioneurotic edema, and neurodermatitis. The cases selected were those in which an allergic cause was suspected. The study was made by taking careful histories and performing intradermal tests and a few patch and passive transfer tests. A total of 12,600 tests were performed; of which 1,237 were positive and 11,287 negative. Of the total number of 12,600 tests, 12,486 were performed intradermally, of which 1,199 were positive and 11,287 negative; 114 tests were performed by the patch method, of which 38 were positive and 76 negative. Eighty-four positive intradermal tests were checked by means of the passive transfer method; of these 36 remained positive, and 50 proved to be negative. Only those to which the patient gave moderate or marked reactions were classed as positive. A little less than half of the cases could be followed for complete study. Sufficient data were obtained, however, to draw the following conclusions:

(1) Intradermal tests are of little value in demonstrating the cause of cutaneous diseases. (2) A great number of positive intradermal reactions are obtained, but they are rarely of practical significance. (3) Positive reactions to food substances or inhalants administered intradermally in patients with cutaneous diseases are far less specific than similar reactions to pollens in patients with hay fever. (4) The indiscriminate subjection of patients with dermatoses to a large number of skin tests is not justifiable. Far greater etiologic help can be obtained by securing a proper history and making a correct derma-

tologic survey. (5) Patch tests are of decided value, especially in cutaneous diseases which are due to external irritants.

Treatment of Allergy with Skin Extract. Köhler, A.: Deutsche med. Wchnschr. **60**: 136, 1934.

The author discusses the treatment of various allergies with specific and nonspecific measures. So far as allergic diseases of the skin are concerned, the use of skin extract as an antigen would be considered to play both a specific and a nonspecific rôle.

The skin extract used was a watery solution of liquid material obtained from skin that had been put through a press. Ten case reports are given, which include bronchial asthma, hay fever, and urticaria, mostly the latter.

The first injection is given 2 c.c. intramuscularly, and may be followed by the same amount intravenously. Injections are increased to 5 c.c. or more intravenously or intramuscularly, according to the symptoms or reactions of the patient treated. These are given at first every day or two and then twice a week. There is no regularity described. They are given up to 10 c.c. intravenously and as often as every day in several cases.

All these patients showed marked improvement, and all of them had been observed for periods of several months. The author reports that a great many more patients have given similar results but have not been observed sufficiently long to form any conclusions. One of these more recent cases is a case of physical allergy with cold urticaria treated with skin extract.

Exophthalmic goiter is a contraindication to these injections.

The author believes that the skin in some way contains immune substances which contribute toward the results obtained. She is encouraged with these results and urges further trial.

Inhalation Therapy in Bronchial Asthma. Welzel, A.: Deutsche med. Wchnschr. **60**: 172, 1934.

The rationale of bringing medication direct to the bronchial mucous membrane is discussed, and various kinds of inhalations are mentioned. The etherial oils, as turpentine, oil of pine, eucalyptus, etc., which are used so commonly to diminish secretions in bronchiectasis, lung abscess, and similar disorders, are contraindicated in bronchial asthma. They not only suppress secretions but also occasionally have a direct spasmodic effect. Likewise, creosote and guaiacol preparations with their bactericidal properties do no good in asthmatic individuals. On the other hand, menthol, which is very commonly employed to allay inflammation, is recommended for nose and throat

disorders which are commonly associated with asthma, although it has no specific effect on the paroxysms.

Preparations containing morphine, atropine, and adrenalin as their principal ingredients are not indicated, as effects from these drugs can be secured when they are given parenterally. "Bronchovydrin" which contains the components papaverin, eumydrin, adrenalin, hypophysis hormone, and nitrite, is a mixture used with success. Also glycerin "silver" is useful in releasing spasm of bronchial muscle and reduction of mucosal swelling. Likewise iodides are useful, but idiosyncrasies to them must be guarded against, and they must not be used in tuberculosis. In general, it may be said that inhalation therapy in bronchial asthma with its complications has much to recommend it as a very effective form of treatment.

Immediate and Late Reactions in Allergic Skin Tests; Their Theoretic and Practical Significance. Tezner, O.: Jahrb. f. Kinderh. **142**: 69, 220, 1934.

In response to primary antigens, such as egg white and horse serum, which are not very toxic, there are two modifications of antibody reaction, namely, the immediate which occurs with a high degree of sensitivity when the antigen is injected either intracutaneously or cutaneously, and the delayed reaction. The immediate reaction occurs characteristically with parenteral sensitization, the delayed with food idiosyncrasies. With several antigens such as serum, there may be a transition from one reaction to another. With dialyzed house dust extract which gave a specific immediate reaction when injected intracutaneously in an asthmatic person, it was not possible to sensitize animals experimentally. This appears to prove the nature of atopens which have been differentiated by Coca.

If one obtains an immediate cutaneous reaction to horse serum either as an obvious allergic response in a sensitive individual or as an inflammatory reaction in an apparently normal subject, an idiosyncrasy to the serum must be presumed. With such an idiosyncrasy (particularly in an asthmatic individual sensitive to horse dander) the injection of even the smallest amount of serum may have severe or even fatal results. It is therefore recommended that if a skin reaction be obtained in any one, that serum be omitted or given with the greatest caution. In arriving at these conclusions an elaborate review of the subject of skin reactions with a very extensive bibliography is given.

Diagnosis of Undulant Fever by Allergic Reaction. Sarnowiec, W.: Compt. rend. Soc. de biol. **115**: 380, 1934.

In his previous work the author showed for the first time the possibility of applying skin tests in the diagnosis of bovine *Brucella*.

The reaction obtained followed the injection of an emulsion of the organisms and this antigen was entirely specific.

In the present work the author has investigated whether the allergic method can be considered as positive, and has used a prophylactic vaccine as an antigen. He obtained two results, depending on the state of the infection present. Two phases of infection exist. The primary, or active, corresponds to the period of invasion which offers more favorable opportunity for a positive diagnostic test. The second, or passive, phase is that in which the bacteria have localized in certain organs. Then the skin reaction is often doubtful. Also if the organisms are extremely attenuated, the host is incapable of developing an intradermal reaction. In this instance the agglutination test is positive. Therefore, one must consider the latter method as the more reliable. As in many other conditions, a negative reaction cannot be necessarily considered absolute.

Book Reviews

ALLERGY AND APPLIED IMMUNOLOGY. WARREN T. VAUGHAN, M.D., Ed. 2, St. Louis, 420 pages, illustrated, The C. V. Mosby Co.

This volume was written as a handbook for physician and patient, and as such contains a great deal of useful information. Unlike many other handbooks, no references are given, but in their place the author from his long experience and opportunity to keep abreast with the subject has interpreted representative opinion for the reader. For the physician, allergy is made understandable by careful explanation, charts, illustrations, and tables. Particular stress is laid on practical points.

Although, as with the first edition, it is felt that the section on applied immunology imparts useful information, its linkage with allergy is not relevant. There is an appendix which is filled with helpful information for both physician and patient.

The second edition is enlarged and revised, and answers many questions about allergy which physicians and patients are wont to ask.

RECENT ADVANCES IN ALLERGY. GEORGE W. BRAY, Ed. 2, Philadelphia, 1934, 502 pages, illustrated, P. Blakiston's Son & Co.

Dr. Bray's book is an excellent compendium which quite completely covers the field of nonbacterial allergy. It goes much farther than its title indicates and includes much that is old as well as new. Its usefulness lies in the fact that essentially every phase of the subject is covered briefly in the text, to which an extensive bibliography is appended. These references are arranged under proper headings at the end of each chapter so that they are easily identified. There is a full index, of both subject matter and authors, which facilitates the identification of the many topics which the book includes.

The second edition is appreciably enlarged, with many sections entirely rewritten and new chapters added. There are likewise new illustrations, which bring the total to 106. As a useful book of reference, it is of much value.